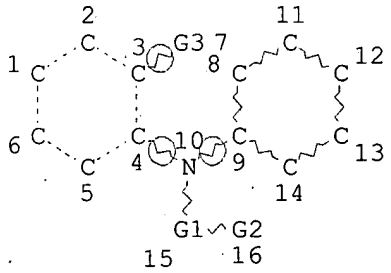
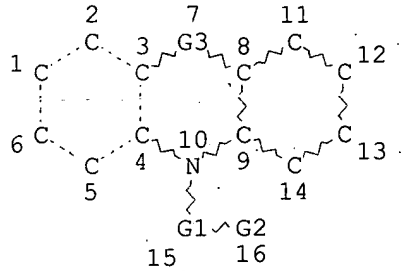
```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:03:30 ON 20 OCT 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1947 - 20 Oct 2001  VOL 135 ISS 18
FILE LAST UPDATED: 19 Oct 2001  (20011019/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

 This file supports REGistRY for direct browsing and searching of
 all substance data from the REGISTRY file.  Enter HELP FIRST for
 more information.

HCAplus now provides online access to patents and literature covered
in CA from 1947 to the present.  On April 22, 2001, bibliographic
information and abstracts were added for over 2.2 million references
published in CA from 1947 to 1966.

=>

=>

=> d stat que l13
L2                STR
```



C @17 A @18

```
REP G1=(4-6) CH2
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/N
VAR G3=17/18
NODE ATTRIBUTES:
NSPEC   IS R      AT  10
NSPEC   IS R      AT  17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  18
```

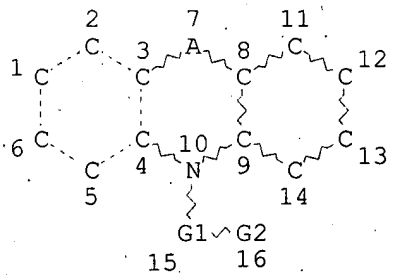
STEREO ATTRIBUTES: NONE
L4 725 SEA FILE=REGISTRY SSS FUL L2
L5 STR



REP G1=(4-6) CH2
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/N
REP G3=(1-10) CH
NODE ATTRIBUTES:
NSPEC IS R AT 10
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

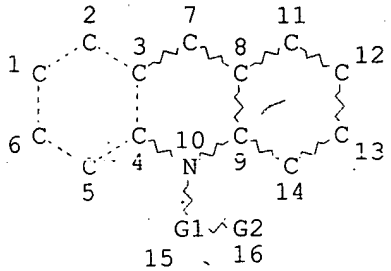
STEREO ATTRIBUTES: NONE
L6 STR



REP G1=(4-6) CH2
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/N
NODE ATTRIBUTES:
NSPEC IS R AT 10
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L8 STR



REP G1=(4-6) CH2
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/N
NODE ATTRIBUTES:
NSPEC IS R AT 10
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

```
L9            98 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L10          468 SEA FILE=REGISTRY SUB=L4 SSS FUL L6 NOT L8
L11           87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
L12          155 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10
L13            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L12
```

=>
=>

=> d ibib abs hitrn l13 1-4

L13 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:512075 HCAPLUS
DOCUMENT NUMBER: 131:286423
TITLE: One-pot synthesis of pharmacologically active diamines via rhodium-catalyzed carbonylative hydroaminomethylation of heterocyclic allylic amines
AUTHOR(S): Rische, Thorsten; Muller, Kai-Sven; Eilbracht, Peter
CORPORATE SOURCE: Organische Chemie I (FB 3), Universitat Dortmund, Dortmund, D-44221, Germany
SOURCE: Tetrahedron (1999), 55(32), 9801-9816
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:286423

AB Pharmacol. active derivs. of phenothiazine, iminodibenzyl, carbazole and pyrazole are prepd. with high yields and chemoselectivity by the reaction of the corresponding N-allylic or N-methallylic compds., primary or secondary amines, carbon monoxide and hydrogen in the presence of [Rh(cod)Cl]2 as catalyst via a one pot hydroformylation-amine condensation-redn. sequence.

IT **2064-12-2P 17261-45-9P 33326-77-1P**

246041-10-1P 246041-11-2P 246041-12-3P
246041-13-4P 246041-14-5P 246041-15-6P
246041-26-9P 246041-27-0P 246041-28-1P
246041-29-2P 246041-30-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(one-pot synthesis of diamines via rhodium-catalyzed carbonylative hydroaminomethylation of heterocyclic allylic amines)

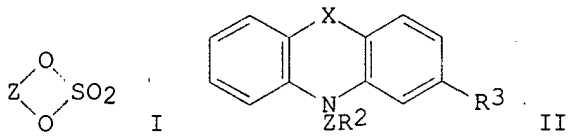
REFERENCE COUNT: 106
REFERENCE(S):
(1) Abou-Gharbia, M; J Med Chem 1987, V30, P1100 HCAPLUS
(4) Barfacker, L; Tetrahedron 1998, P4493 HCAPLUS
(5) Barfacker, L; Tetrahedron 1999, V55, P7177 HCAPLUS
(6) Bayer, A; NL 6505524 1964 HCAPLUS
(8) Bogdal, D; Synth Commun 1997, V27, P1553 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1977:405608 HCAPLUS
DOCUMENT NUMBER: 87:5608
TITLE: Amines and intermediates in their manufacture
INVENTOR(S): Eriksoo, Edgar
PATENT ASSIGNEE(S): Aktiebolag Leo, Swed.
SOURCE: Ger. Offen., 42 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2629945	A1	19770127	DE 1976-2629945	19760702
SE 7607741	A	19770111	SE 1976-7741	19760706
CH 631969	A	19820915	CH 1976-8658	19760706
BE 844018	A1	19770110	BE 1976-168822	19760709
FR 2317275	A1	19770204	FR 1976-21139	19760709
FR 2317275	B1	19810807		
CA 1085824	A1	19800916	CA 1976-256728	19760709
JP 52010201	A2	19770126	JP 1976-81501	19760710
ES 458818	A1	19781101	ES 1977-458818	19770516
US 4249002	A	19810203	US 1978-917923	19780622
US 4249003	A	19810203	US 1978-917924	19780622
CA 1088055	A2	19801021	CA 1979-338959	19791101

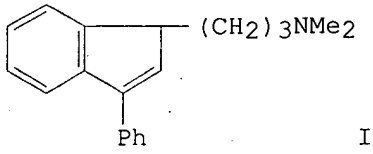
PRIORITY APPLN. INFO.:
GB 1975-29161 19750710
SE 1976-6125 19760517
SE 1976-7741 19760617
US 1976-703534 19760708
CA 1976-256728 19760709
SE 1976-14928 19761126
SE 1976-14929 19761126

GI

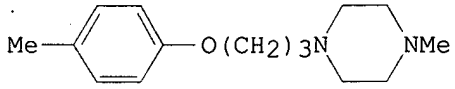


I

II



III



IV

AB Amines RZR1, where RH is a compd. capable of forming a reactive nucleophilic group R-, R1H is an amine, and Z is an alkylene group, were prepd. by treating RM (M = Na, MgBr, Li) with cyclic sulfate I to give RZOSO2M which is treated with R1H. Prepd. were, e.g., II [R2 = NH2, NHMe, NMe2, R3 = H, X = CH:CH, CH2CH2, Z = (CH2)3, (CH2)4; R2 = NHMe, NMe2, 4-hydroxy-1-piperidinyl, 4-methyl-1-piperazinyl, R3 = Cl, CF3, cyano, Ac, MeO, (CH2)3CO, Z = (CH2)3, (CH2)4, X = S], indene III, R(CH2)nR1 (R = Ph2CHO, cyclohexyloxy, PhCH2O, Ph, PhCH2, Ph2CH; R1 = NH2, NHMe, NMe2, n = 2, 3, 4), piperazine IV, N-cyclohexylhexylamine, PhCH2CHPhCH2NH2 (37 compds.), useful as tranquilizers, neuroleptics, and antidepressants (no data). Thus, e.g., 10,11-dihydro-5H-dibenz[b,f]azepine in PhMe was treated under N2 with NaNH2, the mixt. stirred 7 h at 80.degree. and treated with sulfate I [Z = (CH2)3], and the product dibenzazepine II [R2 = OSO2ONa, R3 = H, X = CH2CH2, Z = (CH2)3] treated with aq. MeNH2 6 h at 150.degree. to give II [R2 = NHMe, R3 = H, X = CH2CH2, Z = (CH2)3] as the HCl salt.

IT **2064-12-2P 41743-54-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1968:475445 HCAPLUS
DOCUMENT NUMBER: 69:75445
TITLE: Relation between chemical structure and central N-cholinolytic activity in a series of acetylenic amines and their saturated analogs
AUTHOR(S): Zatsepin, E. P.
CORPORATE SOURCE: Inst. Toksikol., Leningrad, USSR
SOURCE: Farmakol. Toksikol. (1968), 31(4), 431-4
CODEN: FATOAO
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Thirteen acetylenic amines, such as (5,5-diphenylpent-2-ynyl)diethylamine-HCl and I, and their satd. analogs at 0.35 mg./kg. induced nicotine spasma in rabbits. Introduction of a triple bond or a change in the nature of the radical in the hydrocarbon chain did not significantly affect the central N-cholinolytic activity of these compds.

IT **17261-46-0 17261-48-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(parasympatholytic activity of)

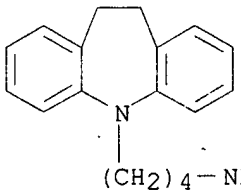
L13 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1968:68866 HCAPLUS
DOCUMENT NUMBER: 68:68866
TITLE: Replacement of labile hydrogen atom by aminoburynyl group
AUTHOR(S): Libman, N. M.; Kuznetsov, S. G.
CORPORATE SOURCE: Inst. Toksikol., Leningrad, USSR
SOURCE: Zh. Org. Khim. (1967), 3(11), 2021-18
CODEN: ZORKAE
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Action of SOCl2 on acetylenic amino alcs. of general formula R2NCH2C.tplbond.CCH2OH (I) gave chlorides R2NCH2C.tplbond.CCH2Cl (II), which were treated with Ph2CR1Na or Ph2CR1K to give Ph2CR1CH2C.tplbond.CCH2NR2 (III), with R22NH to give R22NCH2C.tplbond.CCH2NR2 (IV), or with Ph2CH(OH) to give Ph2CHOCH2C.tplbond.CCH2NR2 (V). Physiol. activity of III, IV, or V analogs had been recorded earlier. Heating .apprx.100.degree. a mixt. of 10 g. HC.tplbond.CCH2OH, 22 g. HNEt2.HCl, 35 ml. HCHO soln., and 1 g. CuCl gave 83% I (R = Et), b15 92-5.degree., n20D 1.4800. In the same way I [(NR2 =) piperidino], b2 120-2.degree., n20D 1.5088, was prepd. in 75% yield. To a soln. of 8 g. I (R = Et) in 20 ml. CH2Cl2 a soln. of 6.75 g. SOCl2 in 5 ml. CH2Cl2 was added and the mixt. kept 1 hr., worked up, and distd. to give 86.5% II (R = Et), b3 63-6.degree., n20D 1.4750 (HCl salt m. 92-3.degree.). Analogously II [(NR2 =) piperidino], b3 92-4.degree., n20D 1.5086, was prepd. To a soln. of KNH2 in liq. NH3 (2.8 g. K, 150 ml. NH3) contg. traces of Fe nitrate a soln. of 12.2 g. Ph2CH2 in 20 ml. Et2O was added followed in 10 min. by II (R = Et). Work-up gave 90.5% III (R = Et, R1 = H), b2 173-4.5.degree., n20D 1.5550 (HCl salt m. 121.5-2.0.degree.). In the same way III (R = Et, R1 = Me), b2 175-7.degree., n20D 1.5555 (HCl salt m. 139-40.degree.), and III (R = Et, R1 = Pr), b1 174-7.degree., n20D 1.5499, were prepd. in 66.5 and 47% yields resp. Reaction of Ph2CR1K with R22NH was carried out in liq. NH3, as above or in Et2O soln., using PhLi, R22NH, and II; the following IV were prepd. (R2N, R22N, % yield, m.p. or b.p./mm., and n20D given): Ph2N, Et2N, 89.5, 177.5-8.degree./2, 1.5775; Ph2N, Et2N, -, -, - (m.p. of tartrate salt 81.5-2.5.degree.); Ph2N, piperidino, 86.5, 192-3.degree./1, 1.5952 (m. HCl salt 173.5-4.degree.); phenothiazino, NEt2, -, -, - (m. HCl salt 133-4.degree.); dibenz[b,f]azepino, NEt2, -, -, - (m. HCl salt 171-1.5.degree.); 2-chlorophenothiazin-10-yl, Net2, -, -, - (HCl salt m. 134.5-5.5.degree., oxalate m. 179.5-80.5.degree.). Reaction between Ph2CHOH and I (R = Et) in liq. NH3 gave 80% V (R = Et), b2 186-6.5.degree., n20D 1.5502 (HCl salt, m. 116.5-17.5.degree.). Hydrogenation of III over PtO2 gave the following satd. diamines R22N(CH2)4NR2 (R22N, R2N, % yield, b.p./mm., n20D, m.p. of HCl salt given): Ph2N, Et2N, 38.5, 173.5.degree./1.5, 1.5665, 138-40.degree.; Ph2N, piperidino, 63.0, 188-9.degree./1, 1.5823, 232-3.degree. (iso-PrOH); phenothiazin-10-yl, Et2N, 36.0, 210.degree./1.5, 1.6100, 131-2.degree. (dioxane); dibenz[b,f]azepin-5-yl, Et2N, 50.5, 200-0.5.degree./2.5, 1.5727, 191.5-2.5.degree..

IT **17261-45-9P 17261-46-0P 17261-47-1P**
17261-48-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

=> select hit rn l13 1-4
E1 THROUGH E18 ASSIGNED

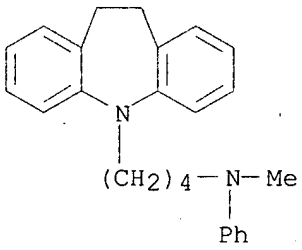
```
=> fil reg
FILE 'REGISTRY' ENTERED AT 14:04:22 ON 20 OCT 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:   19 OCT 2001  HIGHEST RN 363564-17-4
DICTIONARY FILE UPDATES:  19 OCT 2001  HIGHEST RN 363564-17-4

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER see
HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>

=>

=> d his l14

     (FILE 'HCAPLUS' ENTERED AT 14:01:12 ON 20 OCT 2001)

     FILE 'HCAPLUS' ENTERED AT 14:03:30 ON 20 OCT 2001
                SELECT HIT RN L13 1-4

     FILE 'REGISTRY' ENTERED AT 14:04:22 ON 20 OCT 2001
L14            18 S E1-E18

=>
=>

=> d ide can l14 1-18

L14  ANSWER 1 OF 18  REGISTRY  COPYRIGHT 2001 ACS
RN   246041-30-5  REGISTRY
CN   5H-Dibenz[b,f]azepine-5-butanamine, 10,11-dihydro-N-(phenylmethyl)- (9CI)
     (CA INDEX NAME)
FS   3D CONCORD
MF   C25 H28 N2
SR   CA
LC   STN Files:  CA, CAPLUS, CASREACT
```



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

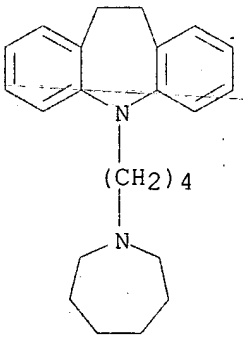
L14 ANSWER 2 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-29-2** REGISTRY
CN 5H-Dibenz[b,f]azepine-5-butanamine, 10,11-dihydro-N-methyl-N-phenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H28 N2
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

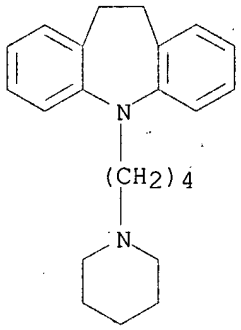
L14 ANSWER 3 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-28-1** REGISTRY
CN 5H-Dibenz[b,f]azepine, 5-[4-(hexahydro-1H-azepin-1-yl)butyl]-10,11-dihydro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H32 N2
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

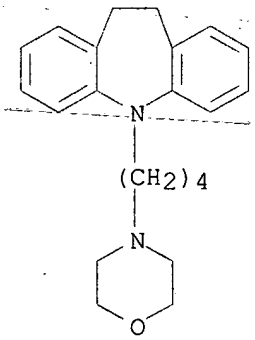
L14 ANSWER 4 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-27-0** REGISTRY
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[4-(1-piperidinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H30 N2
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

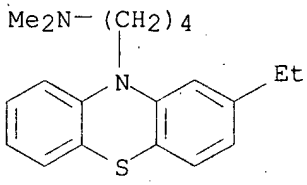
L14 ANSWER 5 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-26-9** REGISTRY
CN 5H-Dibenz[b,f]azepine, 10,11-dihydro-5-[4-(4-morpholinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H28 N2 O
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

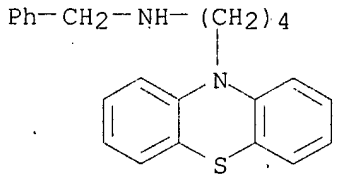
L14 ANSWER 6 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-15-6** REGISTRY
CN 10H-Phenothiazine-10-butanamine, 2-ethyl-N,N-dimethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H26 N2 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

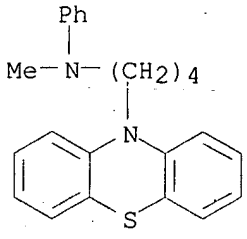
L14 ANSWER 7 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-14-5** REGISTRY
CN 10H-Phenothiazine-10-butanamine, N-(phenylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H24 N2 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

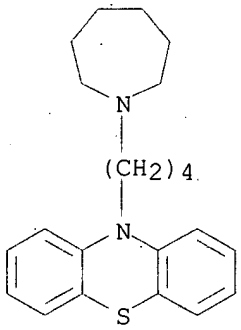
L14 ANSWER 8 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-13-4** REGISTRY
CN 10H-Phenothiazine-10-butanamine, N-methyl-N-phenyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H24 N2 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

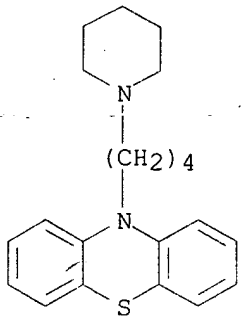
L14 ANSWER 9 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-12-3** REGISTRY
CN 10H-Phenothiazine, 10-[4-(hexahydro-1H-azepin-1-yl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H28 N2 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

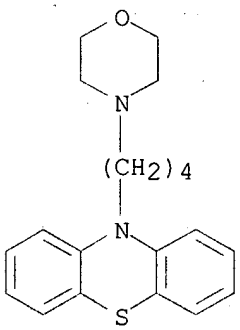
L14 ANSWER 10 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-11-2** REGISTRY
CN 10H-Phenothiazine, 10-[4-(1-piperidinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H26 N2 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

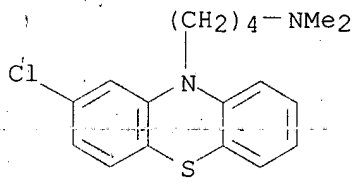
L14 ANSWER 11 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **246041-10-1** REGISTRY
CN 10H-Phenothiazine, 10-[4-(4-morpholinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H24 N2 O S
SR CA
LC STN Files: CA, CAPLUS, CASREACT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

L14 ANSWER 12 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **41743-54-8** REGISTRY
CN 10H-Phenothiazine-10-butanamine, 2-chloro-N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN RP 4684
MF C18 H21 Cl N2 S . Cl H
LC STN Files: BEILSTEIN*, CA, CAPLUS, DDFU, DRUGU, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
CRN (13094-23-0)



● HCl

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 94:20382

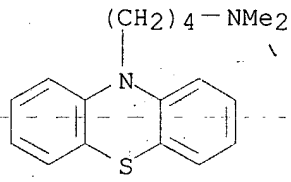
REFERENCE 2: 87:5608

REFERENCE 3: 84:145018

REFERENCE 4: 84:58348

REFERENCE 5: 78:120644

L14 ANSWER 13 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **33326-77-1** REGISTRY
CN 10H-Phenothiazine-10-butanamine, N,N-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenothiazine, 10-[4-(dimethylamino)butyl]- (8CI)
OTHER NAMES:
CN 10-[4-(Dimethylamino)butyl]phenothiazine
FS 3D CONCORD
MF C18 H22 N2 S
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXLIT
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

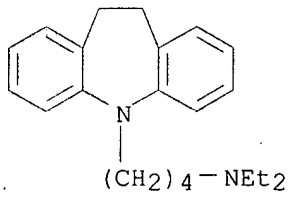
REFERENCE 1: 131:286423

REFERENCE 2: 117:62409

REFERENCE 3: 77:147761

REFERENCE 4: 75:33427

L14 ANSWER 14 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **17261-48-2** REGISTRY
CN 5H-Dibenz[b,f]azepine, 5-[4-(diethylamino)butyl]-10,11-dihydro-, monohydrochloride (8CI) (CA INDEX NAME)
MF C22 H30 N2 . Cl H
LC STN Files: CA, CAPLUS, TOXLIT
CRN (17261-47-1)



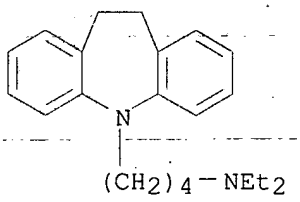
● HCl

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 69:75445

REFERENCE 2: 68:68866

L14 ANSWER 15 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **17261-47-1** REGISTRY
CN 5H-Dibenz[b,f]azepine, 5-[4-(diethylamino)butyl]-10,11-dihydro- (8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H30 N2
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

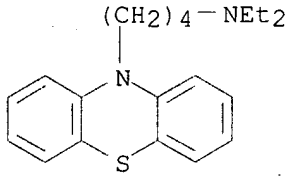


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 68:68866

L14 ANSWER 16 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **17261-46-0** REGISTRY
CN 10H-Phenothiazine-10-butanamine, N,N-diethyl-, monohydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenothiazine, 10-[4-(diethylamino)butyl]-, monohydrochloride (8CI)
MF C20 H26 N2 S . Cl H
LC STN Files: CA, CAPLUS, TOXLIT
CRN (17261-45-9)

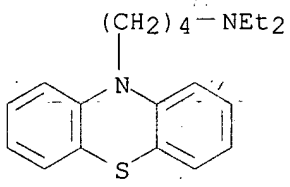


● HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 68:68866

L14 ANSWER 17 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **17261-45-9** REGISTRY
CN 10H-Phenothiazine-10-butanamine, N,N-diethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenothiazine, 10-[4-(diethylamino)butyl]- (8CI)
FS 3D CONCORD
MF C20 H26 N2 S
CI COM
LC STN Files: CA, CAPLUS, CASREACT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

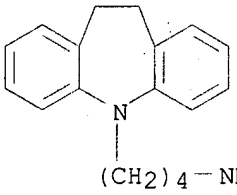
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:286423

REFERENCE 2: 68:95487

REFERENCE 3: 68:68866

L14 ANSWER 18 OF 18 REGISTRY COPYRIGHT 2001 ACS
RN **2064-12-2** REGISTRY
CN 5H-Dibenz[b,f]azepine-5-butanamine, 10,11-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5H-Dibenz[b,f]azepine, 5-[4-(dimethylamino)butyl]-10,11-dihydro- (7CI, 8CI)
OTHER NAMES:
CN N-(Dimethylaminobutyl)iminodibenzene
FS 3D CONCORD
MF C20 H26 N2
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:286423

REFERENCE 2: 128:238900

REFERENCE 3: 87:5608

REFERENCE 4: 82:106183

REFERENCE 5: 71:79388

=>
=>

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:05:56 ON 20 OCT 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1947 - 20 Oct 2001 VOL 135 ISS 18
FILE LAST UPDATED: 19 Oct 2001 (20011019/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

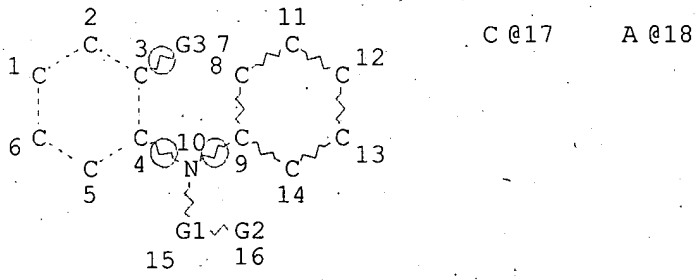
This file supports REGistRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

=>
=>

=> d stat que l15 nos
L2 STR
L4 725 SEA FILE=REGISTRY SSS FUL L2
L5 STR
L9 98 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L15 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L9(L)?MALARIA?

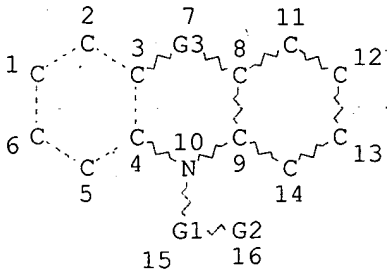
=> d stat que l16
L2 STR



REP G1=(4-6) CH2
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/N
VAR G3=17/18
NODE ATTRIBUTES:
NSPEC IS R AT 10
NSPEC IS R AT 17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L4 725 SEA FILE=REGISTRY SSS FUL L2
L5 STR



```
REP G1=(4-6) CH2
VAR G2=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU/CY/N
REP G3=(1-10) CH
NODE ATTRIBUTES:
NSPEC   IS R      AT  10
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L9            98 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L11           87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
L16            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND ?MALARIA?


=> d stat que l17 nos
L2                STR
L4           725 SEA FILE=REGISTRY SSS FUL L2
L6                STR
L8                STR
L10          468 SEA FILE=REGISTRY SUB=L4 SSS FUL L6 NOT L8
L17            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND ?MALARIA?


=> d stat que l19 nos
L2                STR
L4           725 SEA FILE=REGISTRY SSS FUL L2
L5                STR
L6                STR
L8                STR
L9            98 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L10          468 SEA FILE=REGISTRY SUB=L4 SSS FUL L6 NOT L8
L11           87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
L12          155 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10
L13            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L12
L18           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L11 OR L12)(L)(?PHARM? OR
                  ?MEDICI? OR ?DRUG? OR ?THERAP?)
L19           21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 NOT L13


=>
=>
```

=> d ibib abs hitrn l19 1-21

L19 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:911534 HCAPLUS
DOCUMENT NUMBER: 134:66121
TITLE: Compositions and methods for assaying subcellular conditions and processes using energy transfer for drug screening
INVENTOR(S): Dykens, James A.; Velicelebi, Gonul; Ghosh, Soumitra S.
PATENT ASSIGNEE(S): Mitokor, USA
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000079274	A2	20001228	WO 2000-US17380	20000622
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6280981	B1	20010828	US 2000-514569	20000223

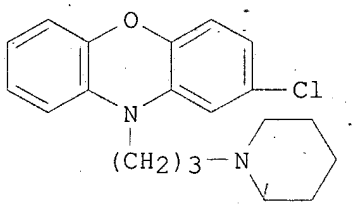
PRIORITY APPLN. INFO.: US 1999-140433 P 19990622
US 1999-338122 A 19990622
US 2000-176383 P 20000114

AB The invention provides compns. and methods for monitoring subcellular compartments such as organelles by energy transfer techniques that do not require specific intermol. affinity binding events between energy transfer donor and energy transfer acceptor mols. pH. Provided are methods for assaying cellular membrane potential, including mitochondrial membrane potential, by energy transfer methodologies including fluorescence resonance energy transfer (FRET). Diagnostic and drug screening assays are also provided.

IT **75168-11-5**, 10-Nonyl acridine orange
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(compns. and methods for assaying subcellular conditions and processes using energy transfer for **drug** screening)

L19 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:780183 HCAPLUS
DOCUMENT NUMBER: 134:110095
TITLE: Synthesis and analysis of structural features of phenoxazine analogues needed to reverse vinblastine resistance in multidrug resistant (MDR) cancer cells
AUTHOR(S): Eregowda, G. B.; Kalpana, H. N.; Hegde, Ravi; Thimmaiah, K. N.
CORPORATE SOURCE: Department of Studies in Chemistry, University of Mysore, Mysore, 570 006, India
SOURCE: Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.

(2000), 39B(4), 243-259
CODEN: IJSBDB; ISSN: 0376-4699
PUBLISHER: National Institute of Science Communication, CSIR
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB To find clin. useful modulators of multidrug resistance (MDR) twenty one 2-chloro-N10-substituted phenoxazines have been synthesized. The novel 2-chlorophenoxazine is prepd. by the pyrolytic condensation of 2-bromophenol and 2,5-dichloronitrobenzene. The lipophilicity expressed in log10P, and pKa of compds. have been detd. All the compds. have been examd. for their ability to increase the uptake of vinblastine (VLB) in MDR KBChR-8-5 cells and the results show that some of the compds. at 100 .mu.M concn. exhibit enhanced accumulation of VLB by 2.0-5.8-fold greater than a similar concn. of verapamil. However, the effects on VLB uptake are specific because these derivs. have little activity in the parental drug-sensitive line KB 3-1. The effect of these compds. on the cellular accumulation of VLB in low P-glycoprotein contg. MDR rhabdomyosarcoma cell line (Rh30) has also been examd. Most of the chlorophenoxazines at 100 .mu.M concn. enhance significantly the accumulation of VLB in Rh30 cells by 10.9-53-fold with respect to control. Substitution of hydrogen with chlorine in position C-2 of the phenoxazine ring increases the ability to enhance the uptake of VLB in KBChR-8-5 cells by 1.15-19.7-fold. The effect of these compds. on the efflux of VLB from KBChR-8-5 cells has been examd. and the results show that most of these compds. significantly inhibit the efflux of VLB consistent with being competitors for P-glycoprotein. Efflux of VLB from Rh30 cells in the presence of 100 .mu.M of some compds. result in 43-65% of the accumulated VLB being retained at 2 h, suggesting that the phenoxazines have relatively little effect on VLB efflux from Rh30 cells. Efflux data in KBChR-8-5 and Rh30 cells suggest that 2-chlorophenoxazines may act through both P-glycoprotein mediated and independent mechanisms. Cytotoxicity has been detd. and the IC50 values lie in the range 3.2-42.1.mu.M for N10-chloropropyl, 2.7-16.7 .mu.M for N10-chlorobutyl and 51.6-68.6 .mu.M for N10-chloroacetyl derivs. against KBChR-8-5 cells suggesting that the antiproliferative activity decreases in the order: - Bu > - Pr > - acetyl analogs. Further, substitution of hydrogen by chlorine in C-2 of phenoxazine ring causes a greater enhancement in the antiproliferative potency by 1.1-2.6-fold for KBChR-8-5 cells than their resp. counterparts, presumably due to increased hydrophobicity. Compds. at IC10 have been evaluated for their efficacy to modulate the cytotoxicity of VLB in KBChR-8-5 cells and compd. I exhibits the greatest MDR reversal effect (136-fold). The structural features for reversal of MDR seem to include a hydrophobic phenoxazine ring with a -Cl group in the C-2 position and a tertiary amino group at a distance of three or four carbon chain from the

tricyclic ring. Examn. of the relation between partition coeff. and cytotoxicity or anti-MDR activity shows no correlation suggesting that lipophilicity is not the sole determinant of potency for biol. activity.

IT **201788-90-1P 201788-92-3P 201788-94-5P**
201788-96-7P 201788-98-9P 201789-00-6P
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and anal. of structural features of phenoxazine analogs needed to reverse vinblastine resistance in **multidrug** resistant (MDR) cancer cells)

REFERENCE COUNT: 37
REFERENCE(S):
(1) Butler, W; Anal Biochem 1984, V141, P70 HCAPLUS
(3) Chauffert, B; Br J Cancer 1987, V56, P119 HCAPLUS
(4) Cornwell, M; FASEB J 1987, V1, P51 HCAPLUS
(5) Cornwell, M; Proc Natl Acad Sci, USA 1986, V83, P3847 HCAPLUS
(7) Deduve, C; Biochem Pharmacol 1974, V23, P2495 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:383927 HCAPLUS
DOCUMENT NUMBER: 133:34425
TITLE: Pharmaceutical compositions containing N-substituted azaheterocyclic compounds for the treatment of indications related to angiogenesis
INVENTOR(S): Hansen, Anker Jon; Jorgensen, Tine Krogh; Olsen, Uffe Bang
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032193	A1	20000608	WO 1999-DK671	19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1135129	A1	20010926	EP 1999-957964	19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: DK 1998-1586 A 19981202
US 1998-111445 P 19981208
WO 1999-DK671 W 19991201
OTHER SOURCE(S): MARPAT 133:34425

AB The present invention relates to the use of N-substituted azaheterocyclic compds. or salts thereof, for the treatment of conditions related to angiogenesis. N-substituted azaheterocyclic compds. decreased the vessel

area of neovascularization of mouse cornea by 30-50%. A tablet contained a N-substituted azaheterocyclic compd. 100, silicone dioxide 1.5, microcryst. cellulose 70, modified cellulose gum 7.5, in the core, and hydroxypropyl Me cellulose 9, and Mywacett 9-40T 0.9 mg in the coating.

IT **170150-06-8**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**pharmaceutical** compns. contg. N-substituted azaheterocyclic compds. for treatment of indications related to angiogenesis)

REFERENCE COUNT: 1
REFERENCE(S): (1) Byeong, M; US 5817678 A 1998 HCAPLUS

L19 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:209026 HCAPLUS
DOCUMENT NUMBER: 133:268
TITLE: Hydrophobic interactions of phenoxazine modulators with bovine serum albumin
AUTHOR(S): Kalpana, H. N.; Channu, B. C.; Dass, Chhabil; Houghton, P. J.; Thimmaiah, K. N.
CORPORATE SOURCE: Department of Studies in Chemistry, University of Mysore, Mysore, 570 006, India
SOURCE: Proc. - Indian Acad. Sci., Chem. Sci. (2000), 112(1), 51-61
CODEN: PIAADM; ISSN: 0253-4134
PUBLISHER: Indian Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interaction of 10-(3'-N-morpholinopropyl)phenoxazine [MPP], 10-(4'-N-morpholinobutyl)phenoxazine [MBP], 10-(3'-N-morpholinopropyl)-2-chlorophenoxazine [MPCP], 10-(3'-N-piperidinopropyl)-2-chlorophenoxazine [PPCP] or 10-(3'-N-morpholinopropyl)-2-trifluoromethylphenoxazine [MPTP] with bovine serum albumin (BSA) has been studied by gel filtration and equil. dialysis methods. The binding of these modulators, based on dialysis expts., has been characterized using the following parameters: percentage of bound drug (.beta.), the assocn. const. (K1), the apparent binding const. (k) and the free energy change (.DELTA.F.degree.). The binding of phenoxazine derivs. to serum transporter protein, BSA, is correlated with their octanol-water partition coeff., log10 P. In addn., effect of the displacing activities of hydroxyzine and acetylsalicylic acid on the binding of phenoxazine derivs. to albumin has been studied. Results of the displacement expts. show that phenoxazine benzene rings and tertiary amines attached to the side chain of the phenoxazine moiety are bound to a hydrophobic area on the albumin mol.

IT **142745-01-5**, 10-(4'-N-Morpholinobutyl)phenoxazine
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(hydrophobic interactions of phenoxazine deriv. **multidrug** resistance modulators with bovine serum albumin)

REFERENCE COUNT: 18
REFERENCE(S): (1) Bird, A; Biochem Pharmacol 1967, V16, P2275 HCAPLUS
(2) Eregowda, G; Asian J Chem 1999, V11, P878 HCAPLUS
(4) Franz, J; Naunyn-Schmiedebergs Arch Pharmakol 1969, V264, P462 HCAPLUS
(5) Giraro, A; US 3048586 1963 HCAPLUS
(7) Hansch, C; J Am Chem Soc 1964, V86, P1616 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:183556 HCAPLUS

DOCUMENT NUMBER: 133:28161
TITLE: Staining of mitochondrial membranes with 10-nonylacridine orange, MitoFluor Green, and MitoTracker Green is affected by mitochondrial membrane potential altering drugs
AUTHOR(S): Keij, Jan F.; Bell-Prince, Carolyn; Steinkamp, John A.
CORPORATE SOURCE: Life Sciences Division, Los Alamos Laboratory, Los Alamos, NM, USA
SOURCE: Cytometry (2000), 39(3), 203-210
CODEN: CYTODQ; ISSN: 0196-4763
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: We set out to develop an assay for the simultaneous anal. of mitochondrial membrane potential and mass using the probes 10-nonyl acridine orange (NAO), MitoFluor Green (MFG), and MitoTracker Green (MTG) in HL60 cells. However, in expts. in which NAO and MFG were combined with orange emitting mitochondrial membrane potential (.DELTA..psi.m) probes, we found clear responses to .DELTA..psi.m altering drugs for both probes. Methods: The three probes were titrated to det. whether satn. played a role in the response to drugs. The effects of a variety of .DELTA..psi.m altering drugs were tested for MFG and MTG at probe concns. of 20 nM and 200 nM and for NAO at 0.1 .mu.M and 5 .mu.M, using rhodamine 123 at 0.1 .mu.M as a ref. probe. Results: Incubation of GM130, HL60, and U937 cells with 2,3-butanedione monoxime (BDM), nigericin, carbonyl cyanide 3-chlorophenylhydrazone (CCCP), carbonyl cyanide p-(trifluoromethoxy)phenylhydrazone (FCCP), 2,4-dinitrophenol (DNP), gramicidin, ouabain, and valinomycin resulted in increases of the fluorescence intensity for MFG or MTG with only a few exceptions. The fluorescence intensity of cells stained with 0.1 .mu.M NAO increased following incubation with BDM, nigericin, and decreased for FCCP, CCCP, DNP, gramicidin, and valinomycin. The results with 5 .mu.M NAO were similar. Conclusions: MFG, MTG, and NAO appeared poor choices for the membrane potential independent anal. of mitochondrial membrane mass. Considering the mol. structure of these probes that favor accumulation in the mitochondrial membrane because of a pos. charge, our results are not surprising.

IT **75168-11-5**, 10-Nonyl acridine orange
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(staining of mitochondrial membranes with 10-nonyl acridine orange MitoFluor Green, and MitoTracker Green is affected by mitochondrial membrane potential altering **drugs**)

REFERENCE COUNT: 26
REFERENCE(S):
(2) Budinger, G; J Biol Chem 1998, V273, P3320 HCAPLUS
(4) Ferlini, C; Cytometry 1995, V21, P284 HCAPLUS
(6) Garner, D; Biol Reprod 1997, V57, P1401 HCAPLUS
(7) Guidot, D; Arch Biochem Biophys 1998, V354, P9 HCAPLUS
(8) Hoth, M; J Cell Biol 1997, V137, P633 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:669501 HCAPLUS
DOCUMENT NUMBER: 132:160896
TITLE: Effect of phenoxazine MDR modulators on photoaffinity labeling of P-glycoprotein by [3H] azidopine: an approach to understand drug resistance in cancer chemotherapy

AUTHOR(S): Kalpana, H. N.; Eregowda, G. B.; Jagadeesh, S.; Thimmaiah, K. N.
CORPORATE SOURCE: Department of Studies in Chemistry, University of Mysore, Mysore, 570 006, India
SOURCE: Indian J. Pharm. Sci. (1999), 61(3), 168-174
CODEN: IJSIDW; ISSN: 0250-474X
PUBLISHER: Indian Pharmaceutical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

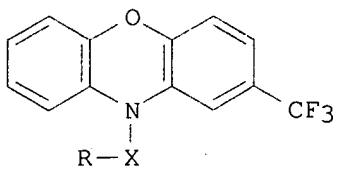
AB Previously, a series of 21 N10-substituted phenoxazines were examd. for reversing vinca alkaloid resistance against MDR KBChR-8-5 and GC3/cl cells. Within the series, there are compds. that inhibit efflux (verapamil-like activity), whereas others markedly increased vinca alkaloid accumulation without having detectable inhibitory activity of the efflux component. It has been shown that MDR modulators that inhibit photoaffinity labeling of P-glycoprotein (P-gp) were generally the most potent MDR reversers. To show whether this observation is true, P-gp rich membrane fractions from KB-V1 cells were isolated and the interaction of [3H] azidopine with membrane fractions in the presence of 25, 50 and 100 .mu.M concn. of each of the twenty N10-substituted phenoxazines was undertaken and the extent of competition was compared to a std. modulator, verapamil. Examn. of the competition data showed that only two modulators exhibited the max. competition (>50%) and the remaining modulators were found to exhibit the inhibition of the photolabeling by less than 45%. However, 3 modulators failed to compete for azidopine labeling. Within the series of compds. examd., the competition of phenoxazines for [3H] azidopine binding to P-gp follows the order: Pr > Bu > acetyl series. It has been found that, from among the compds. examd., three of them interact strongly (>50%), six marginally (<45%) and remaining failed to interact with P-gp, indicating that there may be multiple mechanisms for MDR.

IT **142744-99-8 142745-00-4 142745-01-5**
142745-03-7 142745-04-8 258522-97-3
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of phenoxazine MDR modulators on photoaffinity labeling of p-glycoprotein by [3H] azidopine as approach to understand **drug** resistance in cancer **chemotherapy** and its reversal)

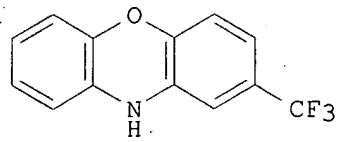
REFERENCE COUNT: 28
REFERENCE(S):
(1) Akiyama, S; Mol Pharmacol 1988, V33, P144 HCAPLUS
(2) Altenberg, G; Am J Physiol 1994, V267, PC1196 HCAPLUS
(4) Beck, W; Biochem Pharmacol 1992, V43, P89 HCAPLUS
(5) Chauffert, B; Br J Cancer 1987, V56, P119 HCAPLUS
(6) Cornwell, M; Proc Natl Acad Sci, USA 1986, V83, P3847 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:466564 HCAPLUS
DOCUMENT NUMBER: 131:228693
TITLE: Structural requirements for activity of phenoxazines for reversal of drug resistance in cancer cells
AUTHOR(S): Eregowda, G. B.; Krishnegowda, G.; Kalpana, H. N.; Channu, B. C.; Dass, C.; Horton, J. K.; Houghton, P. J.; Thimmaiah, K. N.
CORPORATE SOURCE: Department of Studies in Chemistry, University of Mysore, Mysore, 570 006, India
SOURCE: Asian J. Chem. (1999), 11(3), 878-905
CODEN: AJCHEW; ISSN: 0970-7077

PUBLISHER: Asian Journal of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB In the course of a chem. program aimed at identifying chem. useful modulators of MDR in cancer therapy, a series of trifluoromethyl substituted phenoxazines I [R = Et2N, (HOCH2CH2)2N, 4-morpholinyl, 1-piperidinyl, 1-pyrrolidinyl, 4-(2-hydroxyethyl)piperidinyl, Cl; X = (CH2)3, (CH2)4, CH2CO] was prepd. Trifluoromethylphenoxazine II was prepd. by the condensation of 2-bromophenol and 4-chloro-3-nitrobenzotrifluoride in formic acid at 140-160.degree.; II then undergoes N-alkylation under phase transfer conditions with chloroacetyl chloride, 1-bromo-3-chloropropane, or 1-chloro-4-bromobutane to give chloroalkyl intermediates which undergo substitution reactions with amines to give I. II is stirred with 1-bromo-3-chloropropane or 1-bromo-4-chlorobutane in a two phase system of benzene and 6N aq. potassium hydroxide in the presence of tetrabutylammonium bromide to give the intermediates I [X = (CH2)3, (CH2)4; R = Cl] in good yield. Iodide-catalyzed nucleophilic substitution reactions of I [X = (CH2)3, (CH2)4, CH2CO; R = Cl] with secondary amines such as N,N-diethylamine, N,N-diethanolamine, morpholine, piperidine, pyrrolidine and (.beta.-hydroxyethyl)-piperazine yielded the title phenoxazines I. The lipophilicity (as expressed in log10 P) and the pKa of I [R = Et2N, (HOCH2CH2)2N, 4-morpholinyl, 1-piperidinyl, 1-pyrrolidinyl, 4-(2-hydroxyethyl)piperidinyl, Cl; X = (CH2)3, (CH2)4, CH2CO] were detd. The effect of I at 100 .mu.M on the steady-state accumulation of vinblastine (VLB) was studied in KBChR-8-5 cells and the data revealed that phenoxazines I with a Bu linker and most of I contg. a Pr linker exhibited a significant VLB uptake enhancing effect (8.3-58.5-fold relative to control) compared to a std. modulator, verapamil (VRP) (7.5-fold). These eleven compds. caused a 1.10-7.82-fold greater uptake of VLB than did a similar concn. of VRP. Comparison of the derivs. for their ability to potentiate the uptake of VLB revealed that they largely follow the order: N10-Pr > N10-Bu > N10-acetyl compds. To det. whether the increase in VLB uptake upon coincubation with I was due to a slowing of P-gp mediated efflux, KBChR-8-5 cells were loaded with [3H] VLB in the absence of modulator and efflux examd. in the absence or presence of 100 .mu.M of I [X = (CH2)4; R = 4-(2-hydroxyethyl)piperazinyl] or VRP. Less than 10% in the absence or about 40% of cell assocd. VLB in the presence of 100 .mu.M I [X = (CH2)4; R = 4-(2-hydroxyethyl)piperazinyl] remained at the end of a 2 h efflux period, suggesting that I [X = (CH2)4; R = 4-(2-hydroxyethyl)piperazinyl], like VRP, is able to inhibit p-glycoprotein (P-gp) mediated efflux. The cytotoxicities of I were detd. and the IC10 and IC50 values lie resp. in the range 0.1-30.9 .mu.M and 2.1-70.9 .mu.M for KBChR-8-5 cells. Substitution of phenoxazine derivs. with a trifluoromethyl group increases the MDR reversal more effective than other moieties. The partition coeff. and cytotoxicities of I show no correlation, indicating that the hydrophobicity of I is not the sole determinant of biol. activity.

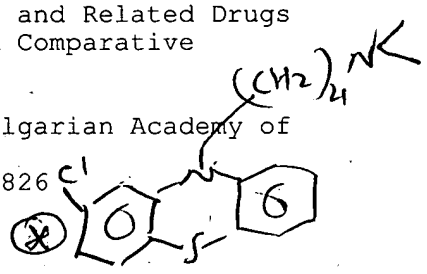
IT **154784-68-6P 244027-36-9P 244027-38-1P**
244027-40-5P 244027-42-7P 244027-44-9P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and cytotoxicity of aminoalkyltrifluoromethylphenoxazines as **multidrug** resistance reversing agents)

REFERENCE COUNT: 40
REFERENCE(S): (1) Bates, S; Am J Pathol 1991, V139, P305 HCAPLUS
(3) Butenandt, A; Ann Chem 1960, V632, P134 HCAPLUS
(4) Butler, W; Analyt Biochem 1984, V141, P70 HCAPLUS
(7) Deduve, C; Biochem Pharmacol 1974, V23, P2495 HCAPLUS
(10) Ford, J; Pharm Rev 1990, V42, P155 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:341171 HCAPLUS
DOCUMENT NUMBER: 129:144642
TITLE: Characterization of 2-chloro-N10-substituted phenoxazines for reversing multidrug resistance in cancer cells
AUTHOR(S): Thimmaiah, Kuntebommanahalli N.; Jayashree, Bullur S.; Germain, Glen S.; Houghton, Peter J.; Horton, Julie K.
CORPORATE SOURCE: Department of Studies in Chemistry, University of Mysore, Mysore, 570006, India
SOURCE: Oncol. Res. (1998), 10(1), 29-41
CODEN: ONREE8; ISSN: 0965-0407
PUBLISHER: Cognizant Communication Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Twenty-one 2-chloro-N10-substituted phenoxazines were characterized as potential modulators of multidrug resistance (MDR). Many of the compds., at a concn. of 100 .mu.M, enhanced accumulation of vinblastine (VLB) in drug-resistant KB8-5 cells to a greater extent than the same concn. of verapamil (VRP). However, the effects on VLB accumulation were specific, because these derivs. had little activity in the parental drug-sensitive line KB3-1. The compds. slowed the efflux of VLB from KB8-5 cells, suggesting that the chlorophenoxazines, like VRP, can inhibit P-glycoprotein (P-gp)-mediated efflux of VLB from this cell line. VRP, 2-chloro-10-[4-(4-morpholinyl)butyl]phenoxazine and 2-chloro-10-(1-piperidinylacetyl)phenoxazine were able to stimulate the vanadate-sensitive ATPase activity attributable to P-gp in membranes isolated from MDR1 baculovirus-infected Sf9 cells. Apparently, these modulators exert their effect by directly interacting with P-gp. Apart from the parent unsubstituted mol., 2-chlorophenoxazine, there was a good correlation between log10P and the ability of the compds. to enhance VLB accumulation in KB8-5. This suggests that lipophilicity of a modulator is important, but is not the sole determinant of potency. Within this series of compds., the optimal structural features for MDR modulation include a hydrophobic phenoxazine ring with a -Cl atom in the C-2 position and a tertiary amine group four carbons from the tricyclic ring. Many of the agents at the IC10 concn. completely reversed the 37-fold VLB resistance in KB8-5 cells. The most active agents in KB8-5 were able to partially reverse VLB resistance in an MDR colon carcinoma cell line GC3/cl and completely reversed the 86-fold VLB resistance in the MDR1-overexpressing breast carcinoma cell line BC19/3. These same agents could only partially sensitize BC19/3 cells to taxol and doxorubicin, suggesting that the chlorophenoxazine derivs. show some specificity for modulating VLB resistance.

IT **201788-90-1 201788-92-3 201788-94-5**
201788-96-7 201788-98-9 201789-00-6
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(2-chloro-N10-substituted phenoxazines for reversing **multidrug** resistance in cancer cells)

L19 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:269997 HCAPLUS
DOCUMENT NUMBER: 128:289904
TITLE: Molecular Modeling of Phenothiazines and Related Drugs As Multidrug Resistance Modifiers: A Comparative Molecular Field Analysis Study
AUTHOR(S): Pajeva, Ilza; Wiese, Michael
CORPORATE SOURCE: Center of Biomedical Engineering, Bulgarian Academy of Sciences, Sofia, BG-1113, Bulg.
SOURCE: J. Med. Chem. (1998), 41(11), 1815-1826
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English



AB A set of 40 phenothiazines, thioxanthenes, and structurally related drugs with multidrug resistance modulating activity in tumor cells in vitro were selected from literature data and subjected to three-dimensional quant. structure-activity relationship study using comparative mol. field anal. (CoMFA). More than 350 CoMFA models were derived and evaluated using steric, electrostatic, and hydrophobic fields alone and in combination. Four alignment strategies based on selected atom pairs or field fit alignment were compared. Several training and test sets were analyzed for both neutral and protonated drug forms sep. Each chem. class was trained and tested individually, and finally the classes were combined together into integrated models. All models obtained were statistically significant and most of them highly predictive. All fields contributed to MDR reversing activity, and hydrophobic fields improved the correlative and predictive power of the models in all cases. The results point to the role of hydrophobicity as a space-directed mol. property to explain differences in anti-MDR activity of the drugs studied.

IT **13094-23-0**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. modeling of phenothiazines, thioxanthene, and related antitumor **drugs** as **multidrug** resistance modifiers by comparative mol. field anal. study)

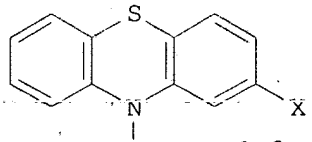
L19 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:49717 HCAPLUS
DOCUMENT NUMBER: 128:162543
TITLE: Drug resistance reversal, antimutagenicity and antiretroviral effect of phthalimido- and chloroethyl-phenothiazines
AUTHOR(S): Motohashi, Noboru; Kurihara, Teruo; Kawase, Masami; Hever, Aniko; Tanaka, Masaru; Szabo, Diana; Nacsa, Janos; Yamanaka, Wataru; Kerim, Ablikim; Molnar, Joseph
CORPORATE SOURCE: Department of Medicinal Chemistry, Meiji College of Pharmacy, Tanashi, 188, Japan
SOURCE: Anticancer Res. (1997), 17(5A), 3537-3543
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: Anticancer Research

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of substituted phenothiazines was studied in three different systems; bacteria and cancer cells and reverse transcriptase enzyme of Moloney leukemia virus. F'lac and hemolysin plasmids were eliminated by some substituted phenothiazines from E. coli at a very low frequency. The same phenothiazine derivs. also were synergistic with tetracycline in bacteria and shown antimutagenic effect in Ames test. No mutagenic effects were obsd. in TA 98 strain of Salmonella typhimunium. Chloroethyl-substituted phenothiazines showed antimutagenicity equiv. to the parent compds.; however, phthalimido-substituted phenothiazines had higher antimutagenicity of 50%. P-glycoprotein responsible for multidrug resistance was also inhibited in tumor cells. The accumulation of the fluorescent rhodamine 123 in the phenothiazine treated multidrug resistant tumor cells was measured by flow cytometry. Some of the substituted phenothiazines were effective P-glycoprotein blockers, while some compds. had moderate activity, but others were without effect as compared to 5 .mu.M verapamil. On the basis of computer anal. there are some correlations between the biol. activities and the dipole moments, and entropy of the studied mols. Our results suggest that the inhibition of Hly+ plasmid replication and P-glycoprotein function may depend partly on similar electronic properties of the studied phenothiazine derivs. The activity of Moloney leukemia virus reverse transcriptase was inhibited by the substituted phenothiazines, however, no basic differences were found in the activities of phthalimido- and chloroethyl substituted phenothiazines.
IT **176657-48-0 180388-72-1**, 1H-Isoindole-1,3(2H)-dione, 2-[4-(10H-phenothiazin-10-yl)butyl]-
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(**drug** resistance reversal, antimutagenicity and antiretroviral effect of phthalimido- and chloroethyl-phenothiazines)

L19 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:916427 HCAPLUS
DOCUMENT NUMBER: 123:313990
TITLE: Antiplasmid phenothiazine derivatives and pharmaceutical compositions containing them
INVENTOR(S): Foldeak, Sandor; Molnar, Jozsef; Petofi, Szilvia
PATENT ASSIGNEE(S): Hung.
SOURCE: Hung. Teljes, 29 pp.
CODEN: HUXXBU
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 66860	A2	19950130	HU 1992-3848	19921204

OTHER SOURCE(S): MARPAT 123:313990
GI



I

AB Disclosed are 10-substituted phenothiazine derivs. I and their salts, where X = halo, H, or trialkylsilyl; R1 and R2 are independently H, C1-6-alkyl, or NR1R2 = 5-7-membered satd. or unsatd. heterocyclic ring which may contain other heteroatoms and which may be substituted with alkylsilylalkyl groups; alk = C2-6 linear or branched alkylene; with the proviso that if R1 = R2 = Me, then alk must be different from C2-3-alkylene. Thus, e.g., phenothiazine was treated with BuLi followed by 1-[(trimethylsilyl)methyl]-4-(2-chloroethyl)piperazine; workup followed by HCl treatment afforded 10-[2-(1-trimethylsilylmethyl-4-piperazinyl)ethyl]phenothiazine.2HCl (75.53% yield) which eliminated 36% of F'lac plasmid at 60 .mu.g/mL from an E. coli K12 LE140 strain, and inhibited R-plasmid transfer to E. coli at 25 .mu.M/mL.

IT **170277-54-0P 170277-55-1P 170277-59-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiplasmid phenothiazine derivs. and **pharmaceutical** compns. contg. them)

L19 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:260681 HCAPLUS
DOCUMENT NUMBER: 120:260681
TITLE: Pharmacological characterization of N-substituted phenoxazines directed toward reversing Vinca alkaloid resistance in multidrug-resistant cancer cells
AUTHOR(S): Horton, Julie K.; Thimmaiah, Kuntebommanahalli N.; Harwood, Franklin C.; Kuttesch, John F.; Houghton, Peter J.
CORPORATE SOURCE: Dep. Mol. Pharamcol., St. Jude Child. Res. Hosp., Memphis, TN, 38105, USA
SOURCE: Mol. Pharmacol. (1993), 44(3), 552-9
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previously the authors reported the synthesis and partial characterization of 21 N10-substituted phenoxazines in reversing Vinca alkaloid resistance. Here, the authors report on a subset of these compds.; the authors have compared their activities in increasing Vinca alkaloid accumulation and reversing drug resistance in KB-ChR8-5 and GC3/c1 (human colon carcinoma) cell lines. Results demonstrated that 1) N-substituted phenoxazinex increase accumulation of vinblastine; 2) within this series, there is little correlation or ranking of activity between the two cell lines when Vinca alkaloid accumulation is compared at equal concns. of modulator; 3) N-substituted phenoxazines demonstrate both quant. and qual. differences, compared with verapamil, a std. modulator; and 4) the series includes at least two compds., 10-[3'-[N-bis(hydroxyethyl)amino]propyl]phenoxazine and 10-(N-piperidinoacetyl)phenoxazine, which increase Vinca alkaloid accumulation but do not significantly inhibit efflux. Addnl., certain of these multidrug resistance modulators significantly enhance accumulation

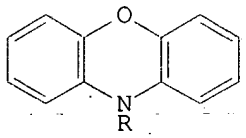
(8-50-fold) of Vinca alkaloids in cell lines with very low or undetectable P-glycoprotein levels, where verapamil has little activity. It is concluded that at least part of the activity of some of these N-substituted phenoxazine modulators may be mediated through a P-glycoprotein-independent mechanism.

IT **142745-00-4 142745-01-5 142745-02-6 142745-03-7 142745-04-8**
RL: BIOL (Biological study)
(Vinca alkaloid resistance reversal by, in **multidrug**-resistant tumor cells of humans)

L19 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:539247 HCAPLUS
DOCUMENT NUMBER: 119:139247
TITLE: Preparation of N-substituted phenoxazines for treating multidrug resistant cancer cells
INVENTOR(S): Houghton, Peter J.; Horton, Julie K.; Thimmaiah, Kuntebommanahalli N.
PATENT ASSIGNEE(S): Research Corp. Technologies, Inc., USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9303729	A1	19930304	WO 1992-US6681	19920810
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
US 5371081	A	19941206	US 1993-126812	19930924

PRIORITY APPLN. INFO.: US 1991-744619 19910812
OTHER SOURCE(S): MARPAT 119:139247
GI

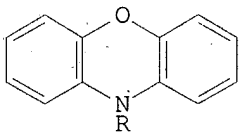


I

AB Title compds. I (R = H, A(CH2)b(CO)a wherein A = (substituted) dialkylamino, substituted heterocyclyl, a = 0, 1; b = 0-6, a + b .noteq. 0) or a salt thereof showing potentiation of antitumor effectiveness of chemotherapeutic agents, particularly in multiple drug resistant cells, are prepd. To NaNH2 in liq. NH3 was added phenoxazine followed by BrCH2CH2CH2Cl to give I (R = Cl(CH2)3). Addn. I was prepd. and evaluated.

IT **142744-99-8P 142745-00-4P 142745-01-5P 142745-02-6P 142745-03-7P 142745-04-8P 142745-11-7P 142745-13-9P 142745-14-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of **multidrug** resistant cancer cells)

L19 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:550951 HCAPLUS
DOCUMENT NUMBER: 117:150951
TITLE: Synthesis and chemical characterization of N-substituted phenoxazines directed toward reversing vinca alkaloid resistance in multidrug-resistant cancer cells
AUTHOR(S): Thimmaiah, Kuntebommanahalli N.; Horton, Julie K.; Seshadri, Ramakrishnan; Israel, Mervyn; Houghton, Janet A.; Harwood, Franklin C.; Houghton, Peter J.
CORPORATE SOURCE: Dep. Biochem. Clin. Pharmacol., St. Jude Child. Res. Hosp., Memphis, TN, 38101, USA
SOURCE: J. Med. Chem. (1992), 35(18), 3358-64
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of N-substituted phenoxazines I [R = (CH2)nR1, COCH2R1, R1 = NEt2, N(CH2CH2OH)2,4-morpholinyl, 1-piperidinyl, 1-pyrrolidinyl, (.beta.-hydroxyethyl)piperazino, n = 3, 4] has been synthesized in an effort to find more specific and less toxic modulators of multidrug resistance (MDR) in cancer chemotherapy. Thus, I [R = (CH2)nCl, COCH2Cl] underwent iodide-catalyzed nucleophilic substitution on reaction with various secondary amines, including N,N-diethylamine, N,N-diethanolamine, morpholine, piperidine, pyrrolidine and (.beta.-hydroxyethyl)piperazine. All of the compds. were examd. for cytotoxicity and for their ability to increase the accumulation of the vinca alkaloids, vincristine (VCR) and vinblastine (VLB) in multidrug-resistant GC3/C1 (human colon adenocarcinoma) and KBChR-8-5 (HeLa variant) cell lines. Compds. were compared to the std. modulator verapamil (VRP). Substitutions on the phenoxazine ring at position 10 were assocd. with an increase in antiproliferative and anti-MDR activities. Modification of the length of the alkyl bridge and the type of amino side chain also influenced the potency of these effects. These modulators, at nontoxic concns., potentiated the cytotoxicity of VCR and VLB in GC3/C1 and KBChR-8-5 cells. Further, I [R = (CH2)nR1, R1 = 4-morpholinyl, n = 3, 4] enhanced accumulation of VLB in GC3/C1, KBChR8-5 and highly resistant KB-V1 cells to a level significantly greater than the maximal level achieved with VRP.

IT **142744-99-8P 142745-00-4P 142745-01-5P**
142745-02-6P 142745-03-7P 142745-04-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and anti-**multidrug** resistance activity of)

L19 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:597616 HCAPLUS
DOCUMENT NUMBER: 115:197616
TITLE: Characterization of multidrug resistance by fluorescent dyes

AUTHOR(S): Kessel, David; Beck, William T.; Kukuruga, Debra; Schulz, Veronique
CORPORATE SOURCE: Dep. Pharmacol., Wayne State Univ., Detroit, MI, 48201, USA
SOURCE: Cancer Res. (1991), 51(17), 4665-70
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fluorimetric techniques were used to examine accumulation of fluorescent probes by the P388 murine leukemia and an anthracycline-resistant subline, P388/Adriamycin (ADR), which expresses the multidrug-resistant phenotype. P388 could be differentiated from P388/ADR on the basis of fluorescence intensity measurements using 3 classes of cationic dyes that are sensitive to membrane potential differences: rhodamine esters, cyanines, and styrylpyridinium dyes. But fluorescence intensity differences were also obsd. with potential-insensitive dyes: zwitterionic rhodamines and an acridine orange deriv. In all cases, fluorescence intensity differences were caused by impaired dye accumulation, and could be eliminated by treatment of P388/ADR cells with verapamil. Moreover, fluorescence signals from 2 anionic potential-sensitive dyes, merocyanine 540 and a bis-oxonol, were identical in P388 and P388/ADR. None of these dyes could be used to delineate CCRF-CEM, and lymphoblastic leukemia of human origin from the CEM/VM-1 subline that exhibits a markedly atypical drug resistance pattern not based on an enhanced outward transport. But accumulation of both neutral and cationic dyes was impaired in CEM/VLB100, a subline of CCRF-CEM expressing mdr. These studies show that many cationic and neutral fluorescent probes are substrates for the enhanced outward drug transport system assocd. with P388/ADR cells, and cannot be used to probe membrane-potential differences in cells expressing the mdr phenotype. With several dyes, difference in fluorescence intensity were sufficient so that flow cytometry could be used to delineate P388 from P388/ADR and CCRF-CEM from CEM-VLB100. The latter technique may be useful for identifying malignant cell populations expressing multidrug resistance in patients with neoplastic disease.

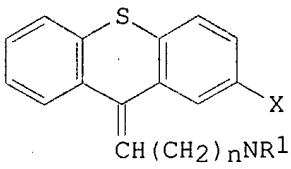
IT **75168-11-5**, A 1372
RL: BIOL (Biological study)
(neoplasm **multidrug** resistance characterization by, as fluorescent probe, in human and lab. animal cells)

L19 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:434686 HCAPLUS
DOCUMENT NUMBER: 113:34686
TITLE: A method of sensitizing multidrug-resistant cells to antitumor agents
INVENTOR(S): Hait, William N.; Ford, James M.
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 361485	A2	19900404	EP 1989-117994	19890928
EP 361485	A3	19901219		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5104858	A	19920414	US 1988-250891	19880929

ZA 8906086	A	19900627	ZA 1989-6086	19890809
JP 02188527	A2	19900724	JP 1989-248236	19890926

PRIORITY APPLN. INFO.: US 1988-250891 19880929
OTHER SOURCE(S): MARPAT 113:34686
GI



I

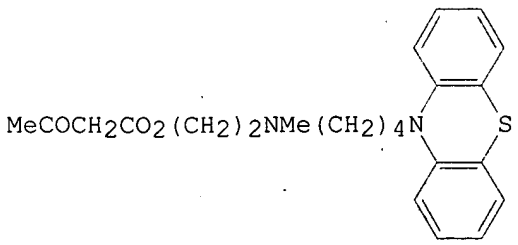
AB Multidrug-resistant cells are sensitized to antitumor agents (e.g., doxorubicin) by exposure to phenothiazines and thioxanthenes (I; X = CF3, OMe, Br, I, Cl, H, or SMe; R1 and R2 = iso-Pr or CH2CH2OHCH2OH; NR1R2 = heterocyclic; n = 0-4). Some structure-activity relations of I as drug sensitizers are described.

IT **13094-23-0**
RL: BIOL (Biological study)
(**multidrug**-resistant neoplasm sensitization by)

L19 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:423083 HCAPLUS
DOCUMENT NUMBER: 111:23083
TITLE: Alk(en)ylenediamine derivatives as intermediates for dihydropyridine derivatives
INVENTOR(S): Ashimori, Atsuyuki; Ono, Taizo; Inoue, Yoshihisa; Fukaya, Tsutomu; Yokoyama, Kazumasa
PATENT ASSIGNEE(S): Green Cross Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63290847	A2	19881128	JP 1987-127734	19870525

OTHER SOURCE(S): MARPAT 111:23083
GI

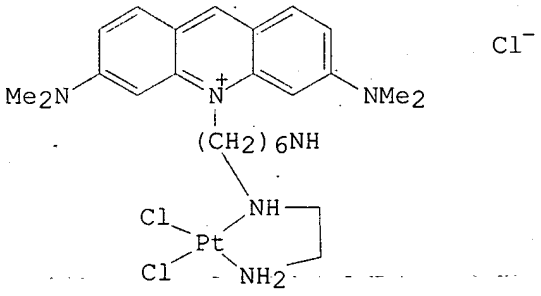


II

AB Title diamines XANR1BNR2R3 [I; X = OH, halo, R4COCH2CO2; R1, R4 = (cyclo or alkoxy)alkyl; R2, R3 = H, alkyl, alkenyl, aralkyl, aryl, heterocyclyl or NR2R3 = heterocyclyl; or R1R2 = ring; A, B = alkylene, alkenylene], as efficient intermediates for pharmaceutical dihydropyridine derivs., are prepd. A prepd. Li phenothiazide soln. was reacted with 1,4-dibromobutane in a THF-HMPA mixt. and the resulting soln. was further reacted with MeHNCH2CH2OH to give 44% of the corresponding phenothiazinylbutylamino deriv. which was esterified with diketene in Et2O to give phenothiazine deriv. II.

IT **116308-72-6P 116308-85-1P 120820-19-1P 120836-32-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as **pharmaceutical**)

L19 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:199676 HCAPLUS
DOCUMENT NUMBER: 104:199676
TITLE: Modulation of platinum antitumor drug binding to DNA by linked and free intercalators
AUTHOR(S): Bowler, Bruce E.; Lippard, Stephen J.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Biochemistry (1986), 25(10), 3031-8
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

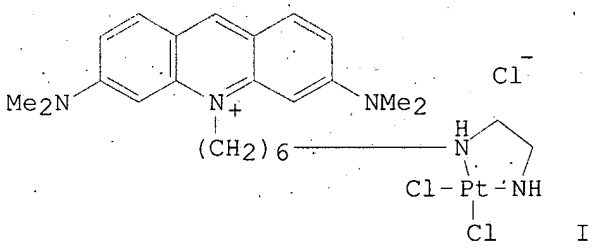


I

AB The DNA-binding site preferences of the novel mol. AO-Pt (I) [**92241-08-2**] is reported. The sequence specificity of Pt binding was mapped by exonuclease III digestion of 165 and 335 base pair restriction fragments from pBR322 DNA. Parallel studies were carried out with the unmodified anticancer **drugs** cis-diamminedichloroplatinum(II) (cis-DDP) [15663-27-1] and chloro(ethylenediamine)platinum(II) [Pt(en)Cl2] [14096-51-6]. Oligo(dG) sequences are the most prevalent binding sites for I, with secondary binding occurring mainly at d(AG) sites. cis-DDP and [Pt(en)Cl2] bind less readily to the secondary sequences, with cis-DDP showing greater binding site selectivity than [Pt(en)Cl2]. The DNA intercalator ethidium bromide [1239-45-8] promotes binding of [Pt(en)Cl2] and cis-DDP to many

sites contg. d(CGG) and, to a lesser extent, d(AG) sequences. AO-Pt exhibits enhanced binding to these sequences without the need for an external intercalator. Unlinked acridine orange [65-61-2], however, does not promote binding of [Pt(en)Cl2] and cis-DDP to d(CGG) and d(AG) sequences. These results are discussed in terms of the sequence preferences, stereochem., and relative residence times of the intercalators at their DNA binding sites. By modulating local structure in a sequence-dependent manner, both linked and, in the case of ethidium, free intercalators can influence the regioselectivity of covalent modification of DNA by Pt antitumor **drugs**.

L19 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1984:563301 HCAPLUS
DOCUMENT NUMBER: 101:163301
TITLE: Synthesis and DNA binding and photonicking properties of acridine orange linked by a polymethylene tether to (1,2-diaminoethane)dichloroplatinum(II)
AUTHOR(S): Bowler, Bruce E.; Hollis, L. Steven; Lippard, Stephen J.
CORPORATE SOURCE: Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: J. Am. Chem. Soc. (1984), 106(20), 6102-4
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The title compd. I [**92241-08-2**] in which both the intercalating functionality and a diammine-coordinated PtCl2 moiety are connected by an appropriate linker chain was prepd. in 9 steps beginning with alkylation of acridine orange [65-61-2] through the intermediate 10-[6-[(2-aminoethyl)amino]hexyl]-3,6-bis(dimethylamino)acridinium chloride-4HCl [**92220-84-3**] and introduction of Pt (K2PtI4) into the chelate ring, and its DNA binding and cleaving (nicking) properties studied. From its binding and light-activated cleaving properties, I may be useful for probing the regiospecificity and stereoselectivity of the binding of Pt antitumor **drugs** to DNA.

L19 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1973:427234 HCAPLUS
DOCUMENT NUMBER: 79:27234
TITLE: Differential effects on mouse brain catechol amine turnover of chlorpromazine, trifluoperazine, and closely-related nontranquilizing analogs
AUTHOR(S): Green, A. L.
CORPORATE SOURCE: Dep. Biochem., Univ. Strathclyde, Glasgow, Scot.

SOURCE: J. Pharm. Pharmacol. (1973), 25(3), 267-9
CODEN: JPPMAB
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chlorpromazine [50-53-3] (20 .mu.mole/kg, s.c.) and trifluoperazine [117-89-5] (10 .mu.mole/kg, s.c.) increased the rate of disappearance of brain noradrenaline [51-41-2] and dopamine [51-61-6] in mice after .alpha.-methyltyrosine treatment. Chlorpromazine had more effect on noradrenaline than on dopamine, whereas trifluoperazine, which is a stronger tranquilizer in man, had a greater effect on dopamine than on noradrenaline. Both **drugs** caused sedation and loss of muscle tone, but these effects were more pronounced in the mice treated with chlorpromazine. In contrast, .alpha.-methyltyrosine-induced depletion of brain catechol amines was not enhanced by either 4-chloro-10-[3-(dimethylamino)propyl]phenothiazine (I) [13094-24-1] (20 .mu.mole/kg, s.c.) or 2-chloro-10-[4-(dimethylamino)butyl]phenothiazine (II) [**13094-23-0**] (20 .mu.mole/kg, s.c.), nor did these **drugs** cause any sedation.

L19 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1972:535105 HCAPLUS
DOCUMENT NUMBER: 77:135105
TITLE: Pharmacological properties of 3-methyl-3,9-diazabicyclo(3.3.1)nonane derivatives of 2-chlorophenothiazine
AUTHOR(S): Medvedev, B. A.; Mashkovskii, M. D.
CORPORATE SOURCE: Lab. Farmakol., Vses. Nauchno-Issled. Khim. Farm. Inst. im. Ordzhonikidze, Moscow, USSR
SOURCE: Farmakol. Toksikol. (Moscow) (1972), 35(4), 401-5
CODEN: FATOAO
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB 3-Methyl-9-[.gamma.-(N-2-chlorophenothiazino)-propyl]-3,9-diazabicyclo[3.3.1]nonane-2-HCl (I) [27447-78-5] exhibited stronger neuroleptic activity in mice and rats than did its butyl or ethyl analog. All 3 homologs increased the duration of phenamine stereotypy in rats.
IT **27447-79-6**
RL: BIOL (Biological study)
(neuroleptic activity and **pharmacol**. of, homologs in relation to)

=> select hitrn l19 1-21
'HITRN' IS NOT A VALID FIELD CODE FOR FILE 'HCAPLUS'
ENTER DISPLAY CODE (TI) OR ?:end

=> select hit rn l19 1-21
E19 THROUGH E53 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:08:45 ON 20 OCT 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 19 OCT 2001 HIGHEST RN 363564-17-4
DICTIONARY FILE UPDATES: 19 OCT 2001 HIGHEST RN 363564-17-4

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER see HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
=>

=> d his l20

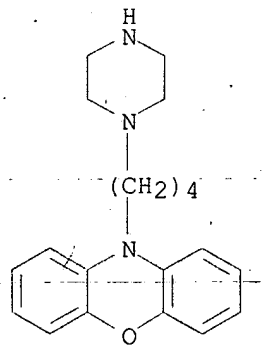
(FILE 'HCAPLUS' ENTERED AT 14:05:56 ON 20 OCT 2001)
SELECT HIT RN L19 1-21

FILE 'REGISTRY' ENTERED AT 14:08:45 ON 20 OCT 2001
L20 35 S E19-E53

=>
=>

=> d ide can l20 1-35

L20 ANSWER 1 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **258522-97-3** REGISTRY
CN 10H-Phenoxazine, 10-[4-(1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H25 N3 O
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

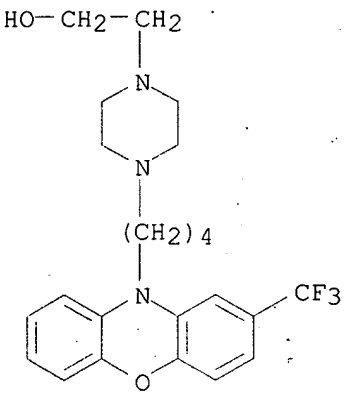


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:160896

L20 ANSWER 2 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **244027-44-9** REGISTRY
CN 1-Piperazineethanol, 4-[4-[2-(trifluoromethyl)-10H-phenoxazin-10-yl]butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H28 F3 N3 O2
SR CA
LC STN Files: CA, CAPLUS

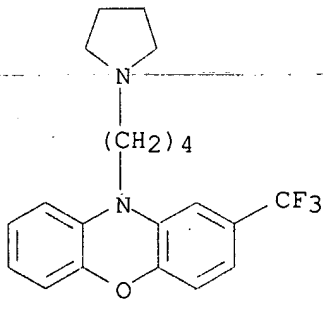


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228693

L20 ANSWER 3 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **244027-42-7** REGISTRY
CN 10H-Phenoxazine, 10-[4-(1-pyrrolidinyl)butyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H23 F3 N2 O
SR CA
LC STN Files: CA, CAPLUS

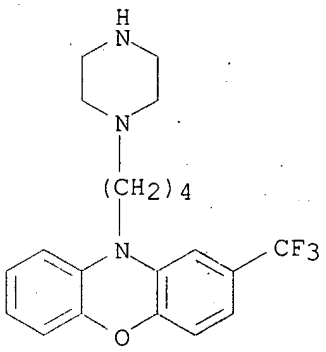


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228693

L20 ANSWER 4 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **244027-40-5** REGISTRY
CN 10H-Phenoxazine, 10-[4-(1-piperazinyl)butyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H24 F3 N3 O
SR CA
LC STN Files: CA, CAPLUS

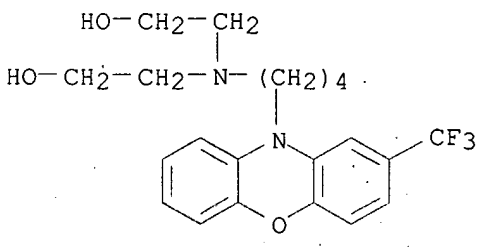


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228693

L20 ANSWER 5 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **244027-38-1** REGISTRY
CN Ethanol, 2,2'-[[4-[2-(trifluoromethyl)-10H-phenoxazin-10-yl]butyl]imino]bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H25 F3 N2 O3
SR CA
LC STN Files: CA, CAPLUS

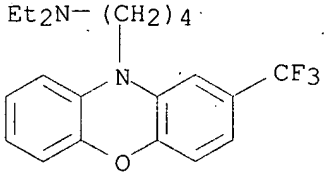


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228693

L20 ANSWER 6 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **244027-36-9** REGISTRY
CN 10H-Phenoxazine-10-butanamine, N,N-diethyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H25 F3 N2 O
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



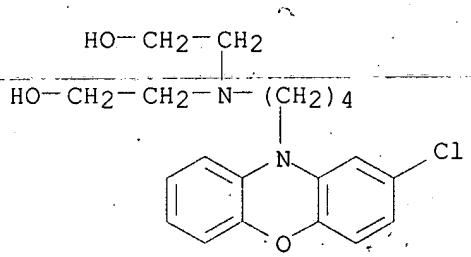
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:289952

REFERENCE 2: 131:228693

L20 ANSWER 7 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **201789-00-6** REGISTRY
CN Ethanol, 2,2'-[[4-(2-chloro-10H-phenoxazin-10-yl)butyl]imino]bis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H25 Cl N2 O3
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)

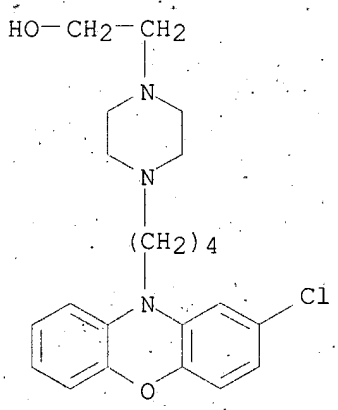
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110095

REFERENCE 2: 129:144642

REFERENCE 3: 128:114649

L20 ANSWER 8 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **201788-98-9** REGISTRY
CN 1-Piperazineethanol, 4-[4-(2-chloro-10H-phenoxazin-10-yl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H28 Cl N3 O2
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

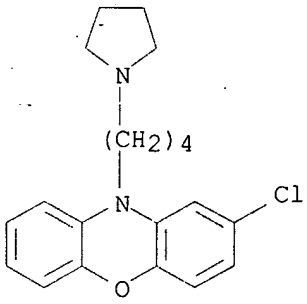
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110095

REFERENCE 2: 129:144642

REFERENCE 3: 128:114649

L20 ANSWER 9 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **201788-96-7** REGISTRY
CN 10H-Phenoxazine, 2-chloro-10-[4-(1-pyrrolidinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H23 Cl N2 O
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

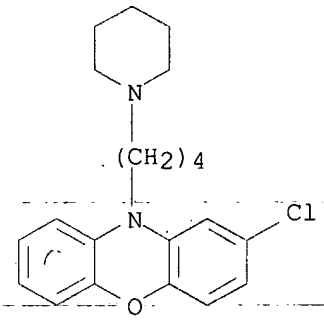
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110095

REFERENCE 2: 129:144642

REFERENCE 3: 128:114649

L20 ANSWER 10 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **201788-94-5** REGISTRY
CN 10H-Phenoxazine, 2-chloro-10-[4-(1-piperidinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H25 Cl N2 O
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

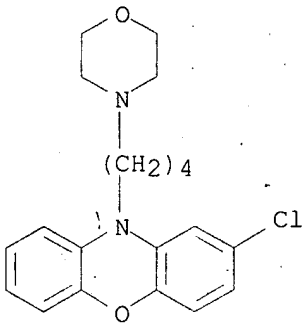
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110095

REFERENCE 2: 129:144642

REFERENCE 3: 128:114649

L20 ANSWER 11 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **201788-92-3** REGISTRY
CN 10H-Phenoxazine, 2-chloro-10-[4-(4-morpholinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H23 Cl N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

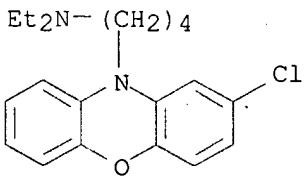
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110095

REFERENCE 2: 129:144642

REFERENCE 3: 128:114649

L20 ANSWER 12 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **201788-90-1** REGISTRY
CN 10H-Phenoxazine-10-butanamine, 2-chloro-N,N-diethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H25 Cl N2 O
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:289952

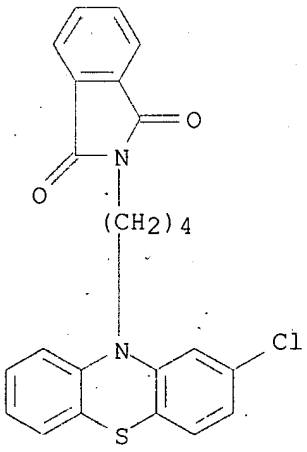
REFERENCE 2: 134:110095

REFERENCE 3: 133:334942

REFERENCE 4: 129:144642

REFERENCE 5: 128:114649

L20 ANSWER 13 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **180388-72-1** REGISTRY
CN 1H-Isoindole-1,3(2H)-dione, 2-[4-(2-chloro-10H-phenothiazin-10-yl)butyl]-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN D 681650
FS 3D CONCORD
MF C24 H19 Cl N2 O2 S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:273829

REFERENCE 2: 132:131770

REFERENCE 3: 129:75984

REFERENCE 4: 128:265747

REFERENCE 5: 128:175800

REFERENCE 6: 128:162631

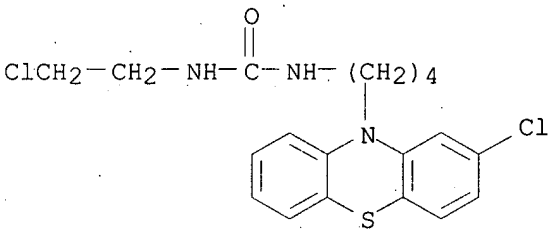
REFERENCE 7: 128:162543

REFERENCE 8: 126:26380

REFERENCE 9: 125:211925

REFERENCE 10: 125:211824

L20 ANSWER 14 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **176657-48-0** REGISTRY
CN Urea, N-(2-chloroethyl)-N'-[4-(2-chloro-10H-phenothiazin-10-yl)butyl]-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN D 681656
FS 3D CONCORD
MF C19 H21 Cl2 N3 O S
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1967 TO DATE)
13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:288297

REFERENCE 2: 132:273829

REFERENCE 3: 132:131770

REFERENCE 4: 129:75984

REFERENCE 5: 128:265747

REFERENCE 6: 128:175800

REFERENCE 7: 128:162631

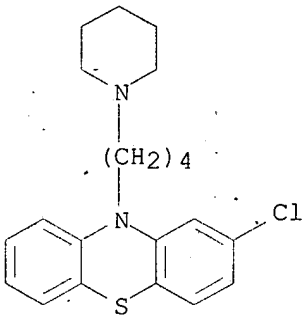
REFERENCE 8: 128:162543

REFERENCE 9: 126:258701

REFERENCE 10: 126:26380

L20 ANSWER 15 OF 35 REGISTRY COPYRIGHT 2001 ACS

RN **170277-59-5** REGISTRY
CN 10H-Phenothiazine, 2-chloro-10-[4-(1-piperidinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H25 Cl N2 S
CI COM
SR CA
LC STN Files: CA, CAPLUS

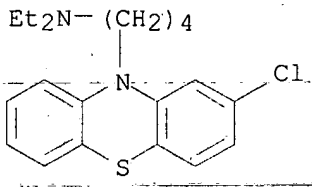


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:313990

L20 ANSWER 16 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **170277-55-1** REGISTRY
CN 10H-Phenothiazine-10-butanamine, 2-chloro-N,N-diethyl-, monohydrochloride (9CI) (CA INDEX NAME)
MF C20 H25 Cl N2 S . Cl H
SR CA
LC STN Files: CA, CAPLUS



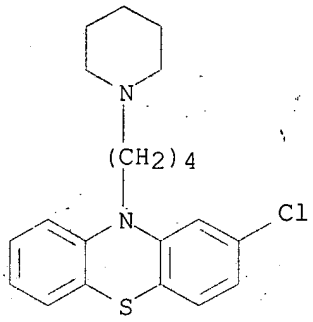
● HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:313990

L20 ANSWER 17 OF 35 REGISTRY COPYRIGHT 2001 ACS

RN **170277-54-0** REGISTRY
CN 10H-Phenothiazine, 2-chloro-10-[4-(1-piperidinyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)
MF C21 H25 Cl N2 S . Cl H
SR CA
LC STN Files: CA, CAPLUS
CRN (170277-59-5)



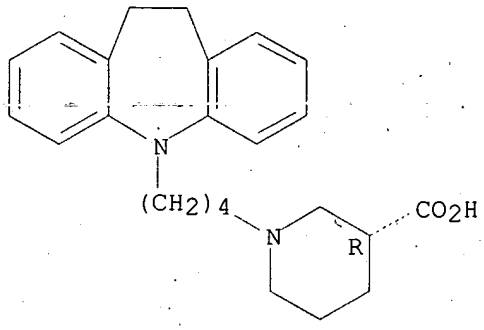
● HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:313990

L20 ANSWER 18 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **170150-06-8** REGISTRY
CN 3-Piperidinecarboxylic acid, 1-[4-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)butyl]-, (3R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Piperidinecarboxylic acid, 1-[4-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)butyl]-, (R)-
FS STEREOSEARCH
MF C24 H30 N2 O2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.



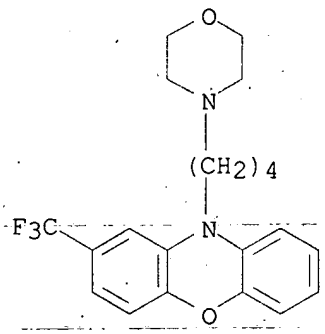
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:34425

REFERENCE 2: 123:313776

L20 ANSWER 19 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **154784-68-6** REGISTRY
CN 10H-Phenoxazine, 10-[4-(4-morpholinyl)butyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H23 F3 N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



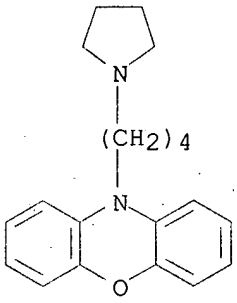
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228693

REFERENCE 2: 120:280030

L20 ANSWER 20 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-14-0** REGISTRY
CN 10H-Phenoxazine, 10-[4-(1-pyrrolidinyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)
MF C20 H24 N2 O . Cl H
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)
CRN (142745-04-8)



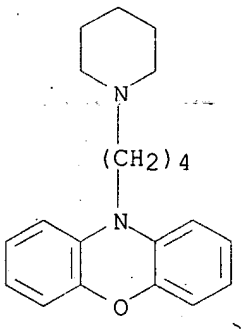
● HCl

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:139247

REFERENCE 2: 117:150951

L20 ANSWER 21 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-13-9** REGISTRY
CN 10H-Phenoxazine, 10-[4-(1-piperidinyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)
MF C21 H26 N2 O . Cl H
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)
CRN (142745-02-6)



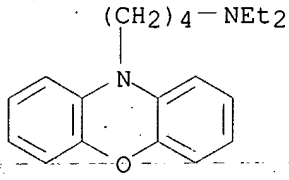
● HCl

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:139247

REFERENCE 2: 117:150951

L20 ANSWER 22 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-11-7** REGISTRY
CN 10H-Phenoxazine-10-butanamine, N,N-diethyl-, monohydrochloride (9CI) (CA INDEX NAME)
MF C20 H26 N2 O . Cl H
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)
CRN (142744-99-8)



● HCl

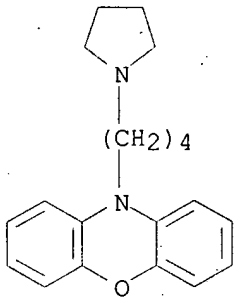
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:139247

REFERENCE 2: 117:150951

L20 ANSWER 23 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-04-8** REGISTRY

CN 10H-Phenoxazine, 10-[4-(1-pyrrolidinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H24 N2 O
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

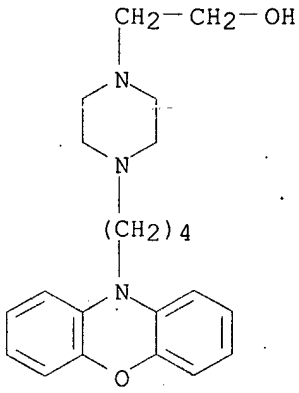
REFERENCE 1: 132:160896

REFERENCE 2: 120:260681

REFERENCE 3: 119:139247

REFERENCE 4: 117:150951

L20 ANSWER 24 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-03-7** REGISTRY
CN 1-Piperazineethanol, 4-[4-(10H-phenoxazin-10-yl)butyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 10H-Phenoxazine, 1-piperazineethanol deriv.
FS 3D CONCORD
MF C22 H29 N3 O2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

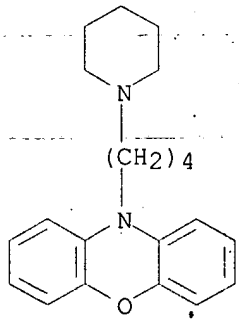
REFERENCE 1: 132:160896

REFERENCE 2: 120:260681

REFERENCE 3: 119:139247

REFERENCE 4: 117:150951

L20 ANSWER 25 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-02-6** REGISTRY
CN 10H-Phenoxazine, 10-[4-(1-piperidinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H26 N2 O
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)

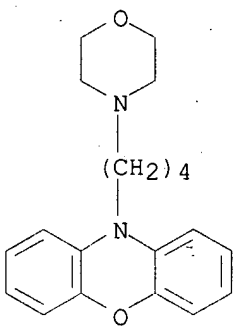
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:260681

REFERENCE 2: 119:139247

REFERENCE 3: 117:150951

L20 ANSWER 26 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-01-5** REGISTRY
CN 10H-Phenoxazine, 10-[4-(4-morpholinyl)butyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H24 N2 O2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:268

REFERENCE 2: 132:160896

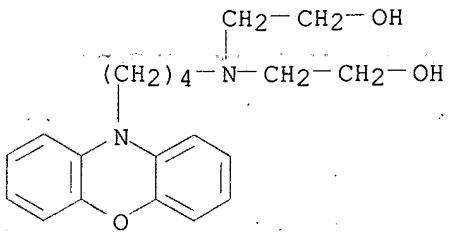
REFERENCE 3: 120:260681

REFERENCE 4: 119:139247

REFERENCE 5: 117:150951

L20 ANSWER 27 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142745-00-4** REGISTRY
CN Ethanol, 2,2'-[[4-(10H-phenoxazin-10-yl)butyl]imino]bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 10H-Phenoxazine, ethanol deriv.
FS 3D CONCORD
MF C20 H26 N2 O3
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

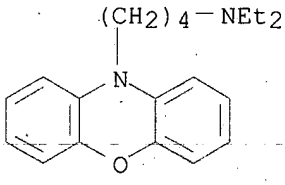
REFERENCE 1: 132:160896

REFERENCE 2: 120:260681

REFERENCE 3: 119:139247

REFERENCE 4: 117:150951

L20 ANSWER 28 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **142744-99-8** REGISTRY
CN 10H-Phenoxazine-10-butanamine, N,N-diethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H26 N2 O
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:160896

REFERENCE 2: 119:139247

REFERENCE 3: 117:150951

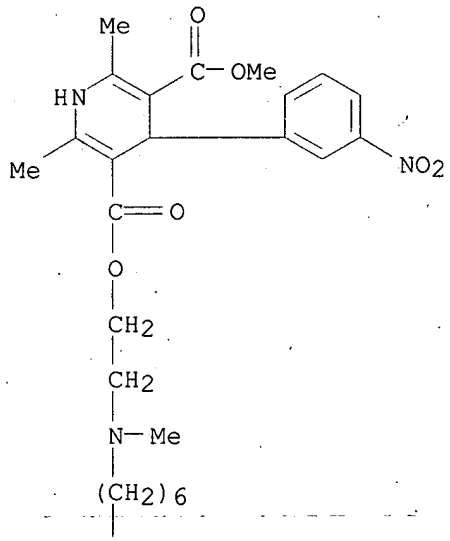
L20 ANSWER 29 OF 35 REGISTRY COPYRIGHT 2001 ACS

RN **120836-32-0** REGISTRY
CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 2-[methyl[6-(10H-phenothiazin-10-yl)hexyl]amino]ethyl ester, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 2-[methyl[6-(10H-phenothiazin-10-yl)hexyl]amino]ethyl ester, (E)-2-butenedioate (1:1)
FS STEREOSEARCH
MF C37 H42 N4 O6 S . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS

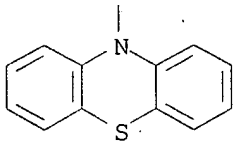
CM 1

CRN 116308-72-6
CMF C37 H42 N4 O6 S

PAGE 1-A



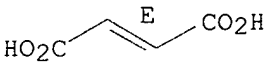
PAGE 2-A



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

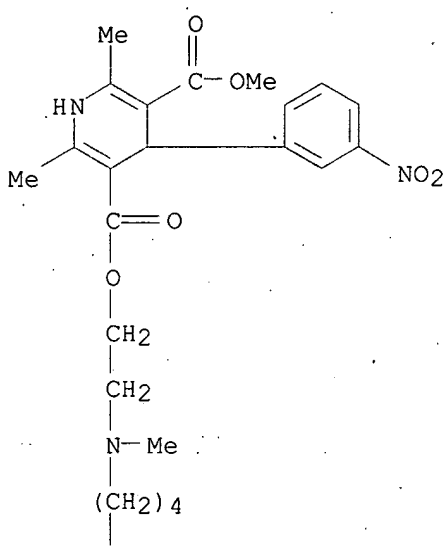
REFERENCE 1: 111:23083

L20 ANSWER 30 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **120820-19-1** REGISTRY
CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 2-[methyl[4-(10H-phenothiazin-10-yl)butyl]amino]ethyl ester, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 2-[methyl[4-(10H-phenothiazin-10-yl)butyl]amino]ethyl ester, (E)-2-butenedioate (1:1)
FS STEREOSEARCH
MF C35 H38 N4 O6 S . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS

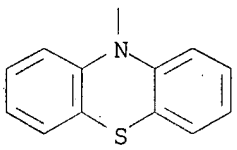
CM 1

CRN 116308-85-1
CMF C35 H38 N4 O6 S

PAGE 1-A



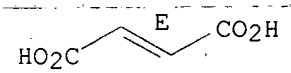
PAGE 2-A



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



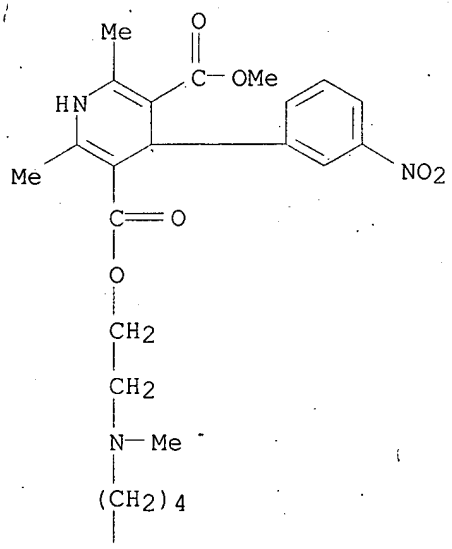
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:23083

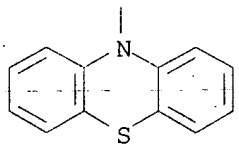
L20 ANSWER 31 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **116308-85-1** REGISTRY
CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-

, methyl 2-[methyl[4-(10H-phenothiazin-10-yl)butyl]amino]ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C35 H38 N4 O6 S
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

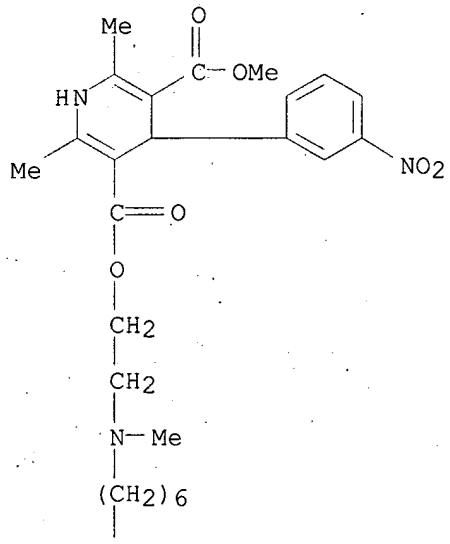
REFERENCE 1: 111:23083

REFERENCE 2: 109:128834

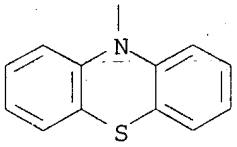
L20 ANSWER 32 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **116308-72-6** REGISTRY

CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-, methyl 2-[methyl[6-(10H-phenothiazin-10-yl)hexyl]amino]ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C37 H42 N4 O6 S
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

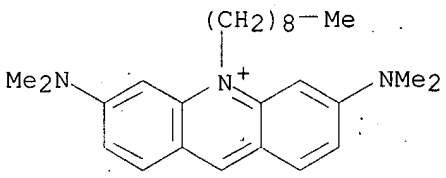
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:23083

REFERENCE 2: 109:128834

L20 ANSWER 33 OF 35 REGISTRY COPYRIGHT 2001 ACS

RN **75168-11-5** REGISTRY
CN Acridinium, 3,6-bis(dimethylamino)-10-nonyl-, bromide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 10-nonyl acridine orange
CN A 1372
MF C26 H38 N3 . Br
LC STN Files: BIOSIS, CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL
CRN (78125-98-1)



14 REFERENCES IN FILE CA (1967 TO DATE)
14 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:231892

REFERENCE 2: 134:66121

REFERENCE 3: 133:319305

REFERENCE 4: 133:174130

REFERENCE 5: 133:28161

REFERENCE 6: 131:56154

REFERENCE 7: 127:328544

REFERENCE 8: 126:207495

REFERENCE 9: 124:305956

REFERENCE 10: 122:163480

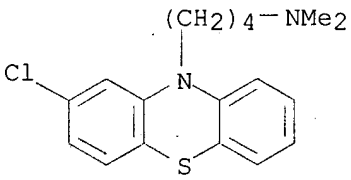
L20 ANSWER 34 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **27447-79-6** REGISTRY
CN 10H-Phenothiazine, 2-chloro-10-[4-(3-methyl-3,9-diazabicyclo[3.3.1]non-9-yl)butyl]-, dihydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,9-Diazabicyclo[3.3.1]nonane, 10H-phenothiazine deriv.
CN Phenothiazine, 2-chloro-10-[4-(3-methyl-3,9-diazabicyclo[3.3.1]non-9-yl)butyl]-, dihydrochloride (8CI)
MF C24 H30 Cl N3 S . 2 Cl H
LC STN Files: BEILSTEIN*, CA, CAPLUS, RTECS*, TOXLIT
(*File contains numerically searchable property data)
CRN (25713-27-3)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 77:135105

REFERENCE 2: 72:132668

L20 ANSWER 35 OF 35 REGISTRY COPYRIGHT 2001 ACS
RN **13094-23-0** REGISTRY
CN 10H-Phenothiazine-10-butanamine, 2-chloro-N,N-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenothiazine, 2-chloro-10-[4-(dimethylamino)butyl]- (7CI, 8CI)
OTHER NAMES:
CN 2-Chloro-10-[4-(dimethylamino)butyl]phenothiazine
CN Butyl chlorpromazine
FS 3D CONCORD
MF C18 H21 Cl N2 S
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

16 REFERENCES IN FILE CA (1967 TO DATE)
16 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 128:289904

REFERENCE 2: 122:281601

REFERENCE 3: 116:120373

REFERENCE 4: 113:204433

REFERENCE 5: 113:34686

REFERENCE 6: 110:107628

REFERENCE 7: 109:85725

REFERENCE 8: 97:192738

REFERENCE 9: 93:161007

REFERENCE 10: 85:56589

```
=>
=>
=> d stat que l21 nos
L2              STR
L4          725 SEA FILE=REGISTRY SSS FUL L2
L5              STR
L6              STR
L8              STR
L9           98 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L10         468 SEA FILE=REGISTRY SUB=L4 SSS FUL L6 NOT L8
L11          87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
L12         155 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10
L13           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L12
L18          21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L11 OR L12)(L)(?PHARM? OR
                ?MEDICI? OR ?DRUG? OR ?THERAP?)
L19          21 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 NOT L13
L21           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L11 OR L12) AND (?FALCIP?
                OR ?SENSITIZ? OR ?PLASMOD? OR ?CHLOROQUIN?)) NOT (L13 OR L19)


=>
=>

=> d ibib abs hitrn l21 1-5

L21  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:227552  HCAPLUS
DOCUMENT NUMBER:          135:19974
TITLE:                    Phenothiazine photosensitizers for onium
                          salt photoinitiated cationic polymerization
AUTHOR(S):                Gomurashvili, Zaza; Crivello, James V.
CORPORATE SOURCE:         Department of Chemistry, Rensselaer Polytechnic
                          Institute, New York State Center for Polymer
                          Synthesis, Troy, NY, 12180, USA
SOURCE:                   J. Polym. Sci., Part A: Polym. Chem. (2001), 39(8),
                          1187-1197
                          CODEN: JPACEC; ISSN: 0887-624X
PUBLISHER:                John Wiley & Sons, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Phenothiazine compds. bearing alkyl and aryl substituents were prepd. and
     evaluated as photosensitizers for photolysis of onium salt
     cationic photoinitiators.  As examples, 10-decylphenothiazine was prepd.
     by direct alkylation of phenothiazine with 1-bromodecane in the presence
     of a base under phase transfer conditions; direct treatment of
     10H-phenothiazine with acetic anhydride under reflux gave
     10-acetylphenothiazine.  These photosensitizers are generally
     operative in the mid- and long-range regions of the UV spectrum and are
     esp. useful for enhancing the rate of photoinitiated cationic polymn.
     carried out utilizing both filtered and broadband UV emission sources.
     The structure and spectral characteristics of the phenothiazines were
     correlated with their efficiency of photosensitization in the
     cationic photopolymns. of several epoxide and vinyl ether monomers.
IT   7516-85-0P, 10-Decylphenothiazine 112686-11-0P,
     10-Decylphenothiazine 5,5-dioxide
     RL: CAT (Catalyst use); SPN (Synthetic preparation); PREP (Preparation);
     USES (Uses)
```

(prepn. and evaluation of substituted phenothiazine as **photosensitizers** for onium salt photoinitiators in cationic polymn. of epoxides and vinyl ethers)

REFERENCE COUNT: 40
REFERENCE(S):
(1) Akhtar, S; J Org Chem 1990, V55, P4222 HCAPLUS
(3) Arnold, D; J Am Chem Soc 1976, V98, P5931 HCAPLUS
(4) Billon, J; Bull Soc Chim France 1960, P1784 HCAPLUS
(5) Bodea, C; Advances in Heterocyclic Chemistry 1968, V9, P321 HCAPLUS
(6) Bradley, G; J Photochem Photobiol A 1996, V100, P109 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:404815 HCAPLUS
DOCUMENT NUMBER: 131:56154
TITLE: Optoacoustic contrast agents and methods for their use in ultrasound and optical imaging
INVENTOR(S): Unger, Evan C.; Wu, Yunqiu
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930620	A1	19990624	WO 1998-US27060	19981217
W: AU, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6123923	A	20000926	US 1997-993165	19971218
AU 9919318	A1	19990705	AU 1999-19318	19981217
EP 1039834	A1	20001004	EP 1998-964127	19981217
R: DE, FR, GB, IT				

PRIORITY APPLN. INFO.: US 1997-993165 A 19971218
WO 1998-US27060 W 19981217

AB The present invention generally relates to optoacoustic contrast agents and methods of diagnostic and therapeutic imaging using optoacoustic contrast agents. A compn. comprising a stabilizing material and a photoactive agent is administered and the patient is scanned using ultrasound imaging and optical imaging to obtain visible images of a region of the patient. The compns. may comprise a wide variety of addnl. components, including, for example, one or more of gases, gaseous precursors, liqs. oils, stabilizing materials, diagnostic agents, photoactive agents, bioactive agents, and/or targeting ligands. Perfluoropropane encapsulated optoacoustic liposomes were formed from dipalmitoylphosphatidylcholine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylethanolamine-PEG 5,000, and dipalmitoylphosphatidylethanolamine derivatized with lissamine rhodamine B. The sized photoactive lipid was optimally excited with 550 nm light and the fluorescence emission peak was 590 nm.

IT **75168-11-5**
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as photoactive agent; optoacoustic contrast agents and methods for

their use in ultrasound and optical imaging)
REFERENCE COUNT: 5
REFERENCE(S): (1) Levy; US 5283255 A 1994 HCAPLUS
(2) Nakakjima, S; Proc SPIE-Int Soc Opt Eng 1995, V2371, P495 HCAPLUS
(3) Unger; US 5846517 A 1998 HCAPLUS
(4) Walters; US 5460800 A 1995
(5) Warren, S; Proc Int Conf Lasers 1993, V15, P795

L21 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:280030 HCAPLUS
DOCUMENT NUMBER: 120:280030
TITLE: Analysis of phenoxazine **chemosensitizers**: an electron ionization and keV-ion beam bombardment mass spectrometry study
AUTHOR(S): Dass, Chhabil; Thimmaiah, K. N.; Jayashree, B. S.; Seshadri, Ramakrishnan; Israel, Mervyn; Houghton, Peter J.
CORPORATE SOURCE: Charles B. Stout Neurosci. Mass Spectrometry, Univ. Tennessee, Memphis, TN, 38163, USA
SOURCE: Biol. Mass Spectrom. (1994), 23(3), 140-6
CODEN: BIMSEH; ISSN: 1052-9306
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mass spectral behavior of a set of eight 2- and 10-disubstituted phenoxazines putatively having anticancer drug enhancer properties was investigated. Both electron ionization (EI) and keV-ion beam bombardment (liq. secondary ion mass spectrometry, LSIMS) were used. As expected, EI led to extensive fragmentation to produce structurally characteristics ions. Except in one example, the mol. ions were reasonably abundant. Two different liq. matrixes - sulfolane and 3-nitrobenzyl alc. - were used to obtain LSIMS data. The use of the latter produced more stable mol. ions. Ion beam bombardment also produced several structure-specific fragments. A unique feature of the LSI spectra obtained using either of the above matrixes is prodn. of both M+. and [M + H]+ ions, with the former being more abundant in most cases. Adduct formation with the liq. matrixes was also obsd. for many compds.
IT **154784-68-6**
RL: PRP (Properties)
(mass spectra of)

L21 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:206326 HCAPLUS
DOCUMENT NUMBER: 114:206326
TITLE: Efficient photoinduced generation of radical cations in solvents of medium and low polarity
AUTHOR(S): Todd, William P.; Dinnocenzo, Joseph P.; Farid, Samir; Goodman, Joshua L.; Gould, Ian R.
CORPORATE SOURCE: Cent. Photoinduced Charge Transfer, Univ. Rochester, Rochester, NY, 14627, USA
SOURCE: J. Am. Chem. Soc. (1991), 113(9), 3601-2
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bimol. photoinduced electron transfer reactions between neutral acceptors and donors are usually performed in polar solvents which allow sepn. within the initially formed radical ion pairs to compete with energy wasting return electron transfer. Since the return electron transfer reactions are often in the Marcus inverted region, their rates should be

significantly reduced in less polar solvents. However, sepn. is inefficient under these conditions due to coulombic attraction within the radical ion pairs. The use of cationic excited state electron acceptors which form neutral radical/radical cation pairs, in which there is no coulombic barrier to sepn. was described. With these **sensitizers**, highly efficient sepn. is obsd. in solvents with a wide range of polarities with quantum yields approaching unity. The utility of such **sensitizers** for steady-state photochem. product formation and for transient absorption expts. is demonstrated. These **sensitizers** should dramatically enhance the scope and utility of photoinduced electron transfer reactions.

IT **132832-87-2**
RL: PRP (Properties)
(**sensitizer**, in photoinduced electron transfer reaction with biphenyl in nonpolar solvents)

L21 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:107628 HCAPLUS
DOCUMENT NUMBER: 110:107628
TITLE: Structural features determining activity of phenothiazines and related drugs for inhibition of cell growth and reversal of multidrug resistance
AUTHOR(S): Ford, James M.; Prozialeck, Walter C.; Hait, William N.
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA
SOURCE: Mol. Pharmacol. (1989), 35(1), 105-15
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Phenothiazines and structurally related compds. inhibit cellular proliferation and **sensitize** multidrug-resistant (MDR) cells to chemotherapeutic agents. To identify more potent pharmaceuticals, the structure-activity relationships of 30 phenothiazines and related compds. on cellular proliferation and MDR in sensitive MCF-7 and resistant MCF-7/DOX human breast cancer cells were studied. Substitutions on the phenothiazine ring that increased hydrophobicity increased antiproliferative and anti-MDR activities. For example, Cl and CF3 groups increased whereas OH groups decreased potency. Modifying the length of the alkyl bridge and the type of amino side chain also influenced potency. Compds. with increased activity against cellular proliferation and MDR possessed a 4-C bridge rather than a 3- or 2-C bridge and a piperazinyl amine rather than a noncyclic amino group. Compds. with tertiary amines were better anti-MDR agents than those with secondary or primary amines but were equipotent antiproliferative agents. The effects of these substituents were unrelated to hydrophobicity. The structure-activity relationships suggest that an ideal phenothiazine structure for reversing MDR has a hydrophobic nucleus with a CF3 ring substitution at position 2, connected by a 4-C alkyl bridge to a para-Me-substituted piperazinyl amine. Related compds. having certain of these properties were subsequently studied. Substitution of a C for an N atom at position 10 of the tricyclic ring, with a double bond to the side chain (thioxanthene), further increased activity against MDR. For example, trans-flupenthixol, the most potent of these compds., increased the potency of doxorubicin against MDR cells by 15-fold, as compared with its stereoisomer cis-flupenthixol (5-fold) or its phenothiazine homolog fluphenazine (3-fold). cis- And trans-flupenthixol were equipotent antiproliferative agents. trans-flupenthixol was not accumulated more than cis-flupenthixol in MDR cells, implying that their stereospecific anti-MDR effects were not the result of selective differences in the access of the drugs to

intracellular targets. Both drugs increased the accumulation of doxorubicin in MDR cells, but not in sensitive cells, suggesting that they modulate MDR by interacting with a uniquely overexpressed cellular target in these resistant cells. The apparent lack of clin. toxicity of trans-flupenthixol makes it an attractive drug for further investigation.
IT 13094-23-0, 2-Chloro-10-[4-(dimethylamino)butyl]phenothiazine
RL: BIOL (Biological study)
(cytotoxicity of and neoplasm inhibitor resistance reversal by, in human cells, structure in relation to)

=>
=>

=> select hit rn l21 1-5
E54 THROUGH E59 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:14:03 ON 20 OCT 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 19 OCT 2001 HIGHEST RN 363564-17-4
DICTIONARY FILE UPDATES: 19 OCT 2001 HIGHEST RN 363564-17-4

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER see HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
=>

=> d his l22

(FILE 'HCAPLUS' ENTERED AT 14:11:29 ON 20 OCT 2001)
SELECT HIT RN L21 1-5

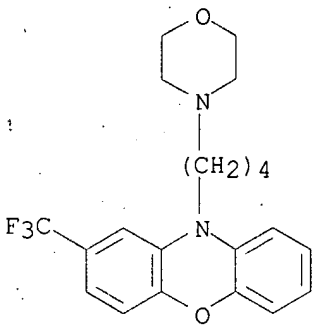
FILE 'REGISTRY' ENTERED AT 14:14:03 ON 20 OCT 2001
L22 6 S E54-E59

=>
=>

=> d ide can l22 1-6

L22 ANSWER 1 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **154784-68-6** REGISTRY
CN 10H-Phenoxazine, 10-[4-(4-morpholinyl)butyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

FS 3D CONCORD
MF C21 H23 F3 N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

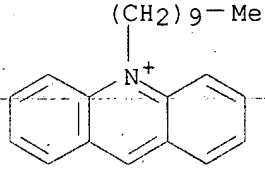
REFERENCE 1: 131:228693

REFERENCE 2: 120:280030

L22 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **132832-87-2** REGISTRY
CN Acridinium, 10-decyl-, hexafluorophosphate(1-) (9CI) (CA INDEX NAME)
MF C23 H30 N . F6 P
SR CA
LC STN Files: CA, CAPLUS

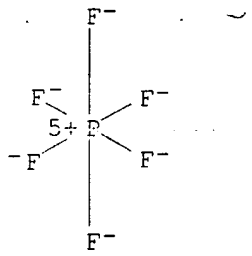
CM 1

CRN 132832-86-1
CMF C23 H30 N



CM 2

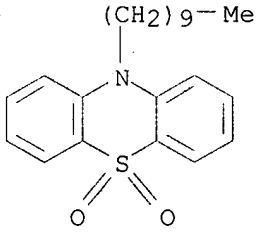
CRN 16919-18-9
CMF F6 P
CCI CCS



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 114:206326

L22 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **112686-11-0** REGISTRY
CN 10H-Phenothiazine, 10-decyl-, 5,5-dioxide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenothiazine, 10-decyl-, 5,5-dioxide (6CI)
OTHER NAMES:
CN 10-Decylphenothiazine 5,5-dioxide
FS 3D CONCORD
MF C22 H29 N O2 S
SR CAOLD
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMCATS
(*File contains numerically searchable property data)

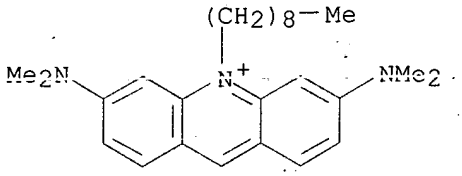


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:19974

L22 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **75168-11-5** REGISTRY
CN Acridinium, 3,6-bis(dimethylamino)-10-nonyl-, bromide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 10-nonyl acridine orange
CN A 1372
MF C26 H38 N3 . Br
LC STN Files: BIOSIS, CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL
CRN (78125-98-1)



● Br^-

14 REFERENCES IN FILE CA (1967 TO DATE)
14 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:231892

REFERENCE 2: 134:66121

REFERENCE 3: 133:319305

REFERENCE 4: 133:174130

REFERENCE 5: 133:28161

REFERENCE 6: 131:56154

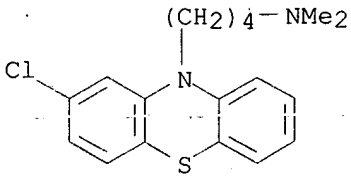
REFERENCE 7: 127:328544

REFERENCE 8: 126:207495

REFERENCE 9: 124:305956

REFERENCE 10: 122:163480

L22 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **13094-23-0** REGISTRY
CN 10H-Phenothiazine-10-butanamine, 2-chloro-N,N-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenothiazine, 2-chloro-10-[4-(dimethylamino)butyl]- (7CI, 8CI)
OTHER NAMES:
CN 2-Chloro-10-[4-(dimethylamino)butyl]phenothiazine
CN Butyl chlorpromazine
FS 3D CONCORD
MF C18 H21 Cl N2 S
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

16 REFERENCES IN FILE CA (1967 TO DATE)
16 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 128:289904

REFERENCE 2: 122:281601

REFERENCE 3: 116:120373

REFERENCE 4: 113:204433

REFERENCE 5: 113:34686

REFERENCE 6: 110:107628

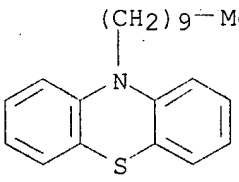
REFERENCE 7: 109:85725

REFERENCE 8: 97:192738

REFERENCE 9: 93:161007

REFERENCE 10: 85:56589

L22 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **7516-85-0** REGISTRY
CN 10H-Phenothiazine, 10-decyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenothiazine, 10-decyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 10-Decylphenothiazine
CN N-Decylphenothiazine
FS 3D CONCORD
MF C22 H29 N S
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMCATS
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:53434

REFERENCE 2: 135:19974

REFERENCE 3: 133:357152

REFERENCE 4: 133:335005

REFERENCE 5: 133:288647

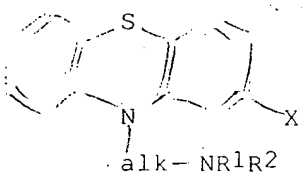
REFERENCE 6: 131:136657

REFERENCE 7: 121:121535

L19 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:916427 HCAPLUS
DOCUMENT NUMBER: 123:313990
TITLE: Antiplasmid phenothiazine derivatives and pharmaceutical compositions containing them
INVENTOR(S): Foldeak, Sandor; Molnar, Jozsef; Petofi, Szilvia
PATENT ASSIGNEE(S): Hung.
SOURCE: Hung. Teljes, 29 pp.
CODEN: HUXXBU
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 66860	A2	19950130	HU 1992-3848	19921204

OTHER SOURCE(S): MARPAT 123:313990
GI

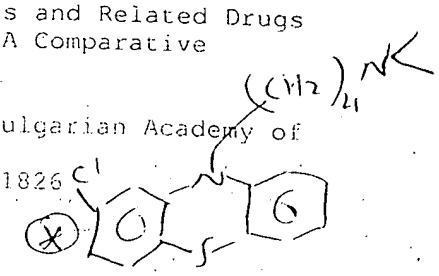


I

AB Disclosed are 10-substituted phenothiazine derivs. I and their salts, where X = halo, H, or trialkylsilyl; R1 and R2 are independently H, C1-6-alkyl, or NR1R2 = 5-7-membered satd. or unsatd. heterocyclic ring which may contain other heteroatoms and which may be substituted with alkylsilylalkyl groups; alk = C2-6 linear or branched alkylene; with the proviso that if R1 = R2 = Me, then alk must be different from C2-3-alkylene. Thus, e.g., phenothiazine was treated with BuLi followed by 1-[(trimethylsilyl)methyl]-4-(2-chloroethyl)piperazine; workup followed by HCl treatment afforded 10-[2-(1-trimethylsilylmethyl-4-piperazinyl)ethyl]phenothiazine.2HCl (75.53% yield) which eliminated 36% of F'lac plasmid at 60 .mu.g/mL from an E. coli K12 LE140 strain, and inhibited R-plasmid transfer to E. coli at 25 .mu.M/mL.

IT **170277-54-0P 170277-55-1P 170277-59-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiplasmid phenothiazine derivs. and **pharmaceutical** compns. contg. them)

L19 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:269997 HCAPLUS
DOCUMENT NUMBER: 128:289904
TITLE: Molecular Modeling of Phenothiazines and Related Drugs As Multidrug Resistance Modifiers: A Comparative Molecular Field Analysis Study
AUTHOR(S): Pajeva, Ilza; Wiese, Michael
CORPORATE SOURCE: Center of Biomedical Engineering, Bulgarian Academy of Sciences, Sofia, BG-1113, Bulg.
SOURCE: J. Med. Chem. (1998), 41(11), 1815-1826
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English



AB A set of 40 phenothiazines, thioxanthenes, and structurally related drugs with multidrug resistance modulating activity in tumor cells in vitro were selected from literature data and subjected to three-dimensional quant. structure-activity relationship study using comparative mol. field anal. (CoMFA). More than 350 CoMFA models were derived and evaluated using steric, electrostatic, and hydrophobic fields alone and in combination. Four alignment strategies based on selected atom pairs or field fit alignment were compared. Several training and test sets were analyzed for both neutral and protonated drug forms sep. Each chem. class was trained and tested individually, and finally the classes were combined together into integrated models. All models obtained were statistically significant and most of them highly predictive. All fields contributed to MDR reversing activity, and hydrophobic fields improved the correlative and predictive power of the models in all cases. The results point to the role of hydrophobicity as a space-directed mol. property to explain differences in anti-MDR activity of the drugs studied.

IT 13094-23-0
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. modeling of phenothiazines, thioxanthene, and related antitumor **drugs** as **multidrug** resistance modifiers by comparative mol. field anal. study)